

10/717,958

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10/717,958

AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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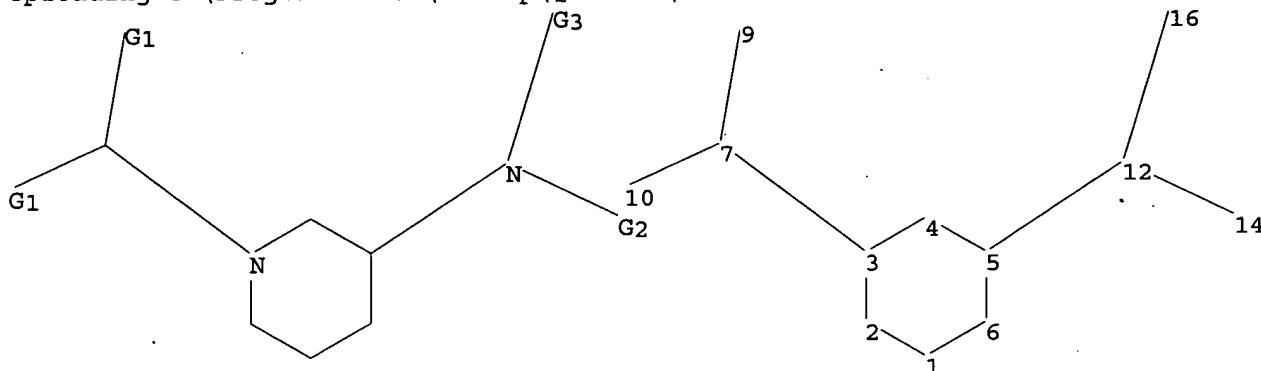
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*****
* The CA roles and document type information have been removed from *
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chain nodes :

7 9 10 12 14 16

ring nodes :

1 2 3 4 5 6

chain bonds :

3-7 5-12 7-9 7-10 12-14 12-16

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

1-2 1-6 2-3 3-4 3-7 4-5 5-6 5-12 7-9 7-10 12-14 12-16

isolated ring systems :

containing 1 :

G1:H,O

G2:H,O,S,Cb,Ak

G3:H,Cb,Ak

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 9:CLASS 10:CLASS
12:CLASS 14:CLASS 16:CLASS

L1 STRUCTURE UPLOADED

=> s 11
SAMPLE SEARCH INITIATED 12:08:24 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 2331 TO ITERATE

85.8% PROCESSED 2000 ITERATIONS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

50 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 43724 TO 49516
PROJECTED ANSWERS: 4782 TO 6826

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L2 50 SEA SSS SAM L1

=> s 11 ful
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FULL SCREEN SEARCH COMPLETED - 47505 TO ITERATE

100.0% PROCESSED 47505 ITERATIONS 6103 ANSWERS
SEARCH TIME: 00.00.01

L3 6103 SEA SSS FUL L1

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FULL ESTIMATED COST ENTRY SESSION
161.33. 161.54

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FILE COVERS 1907 - 6 Sep 2005 VOL 143 ISS 11
FILE LAST UPDATED: 5 Sep 2005 (20050905/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13
L4 1211 L3

=> s 14 and (process or procedure or make or synthes? or made or method)
2141802 PROCESS
1431639 PROCESSES
3185804 PROCESS
(PROCESS OR PROCESSES)
418659 PROCEDURE
178953 PROCEDURES
572259 PROCEDURE
(PROCEDURE OR PROCEDURES)
215270 MAKE
167192 MAKES
371370 MAKE
(MAKE OR MAKES)
1473235 SYNTHES?
1164781 MADE

10/717, 958

24 MADES
1164802 MADE
(MADE OR MADES)

2932792 METHOD
1206963 METHODS
3800247 METHOD
(METHOD OR METHODS)

L5 473 L4 AND (PROCESS OR PROCEDURE OR MAKE OR SYNTHES? OR MADE OR
METHOD)

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3 REDUCINGS
329101 REDUCING
(REDUCING OR REDUCINGS)
743483 AGENT
1071342 AGENTS
1513325 AGENT
(AGENT OR AGENTS)
58478 REDUCING AGENT
(REDUCING (W) AGENT)

L6 0 L5 AND REDUCING AGENT

=> s 15 and (reducing or reduce or reduction)

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296642 REDUCTION
5383 REDUCTIONS
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(REDUCTION OR REDUCTIONS)
863249 REDN
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892920 REDN
(REDN OR REDNS)

1026206 REDUCTION
(REDUCTION OR REDN)

L7 68 L5 AND (REDUCING OR REDUCE OR REDUCTION)

=> s 17 and (borohydride or lithium aluminum)

20350 BOROHYDRIDE
1327 BOROHYDRIDES
20780 BOROHYDRIDE
(BOROHYDRIDE OR BOROHYDRIDES)

295210 LITHIUM
358 LITHIUMS
295334 LITHIUM
(LITHIUM OR LITHIUMS)

888883 ALUMINUM
297 ALUMINUMS
888944 ALUMINUM
(ALUMINUM OR ALUMINUMS)

9225 LITHIUM ALUMINUM
(LITHIUM (W) ALUMINUM)

L8 4 L7 AND (BOROHYDRIDE OR LITHIUM ALUMINUM)

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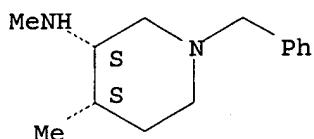
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L8 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:909780 CAPLUS
DOCUMENT NUMBER: 138:137134
TITLE: Development of a Scaleable Route for the Production of cis-N-Benzyl-3-methylamino-4-methylpiperidine
AUTHOR(S): Ripin, David H. Brown; Abele, Stefan; Cai, Weiling; Blumenkopf, Todd; Casavant, Jeffrey M.; Doty, Jonathan L.; Flanagan, Mark; Koecher, Christian; Laue, Klaus W.; McCarthy, Keith; Meltz, Cliff; Munchhoff, Mike; Pouwer, Kees; Shah, Bharat; Sun, Jianmin; Teixeira, John; Vries, Ton; Whipple, David A.; Wilcox, Glenn
CORPORATE SOURCE: Chemical Research and Development Pfizer Global Research Division, Pfizer Inc., Groton, CT, 06340, USA
SOURCE: Organic Process Research & Development (2003), 7(1), 115-120
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:137134

IT 477600-68-3P
RL: IMF (Industrial manufacture); PREP (Preparation)
(large-scale stereoselective preparation of cis-1-benzyl-4-methyl-3-(methylamino)piperidine)

RN 477600-68-3 CAPLUS
CN 3-Piperidinamine, N,4-dimethyl-1-(phenylmethyl)-, dihydrochloride,
(3R,4R)-rel- (9CI) (CA INDEX NAME)

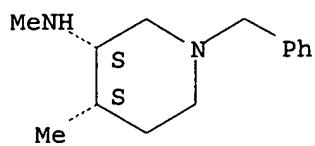
Relative stereochemistry.



● 2 HCl

IT 477600-69-4P
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(large-scale stereoselective preparation of cis-1-benzyl-4-methyl-3-(methylamino)piperidine)
RN 477600-69-4 CAPLUS
CN 3-Piperidinamine, N,4-dimethyl-1-(phenylmethyl)-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 493040-24-7P

RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
 (resolution in the large-scale stereoselective preparation of nonracemic
 cis-1-benzyl-4-methyl-3-(methylamino)piperidine)

RN 493040-24-7 CAPLUS

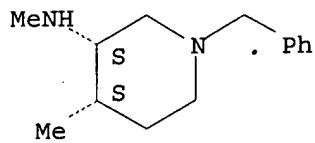
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with
 rel-(3R,4R)-N,4-dimethyl-1-(phenylmethyl)-3-piperidinamine (1:2) (9CI)
 (CA INDEX NAME)

CM 1

CRN 477600-69-4

CMF C14 H22 N2

Relative stereochemistry.

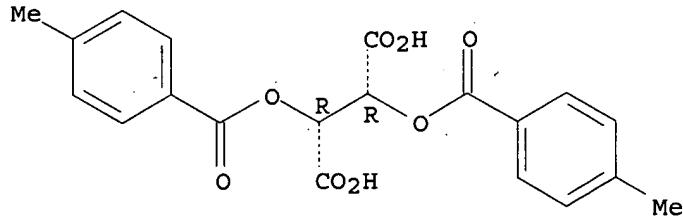


CM 2

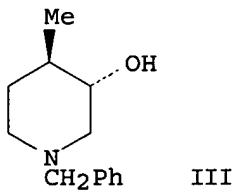
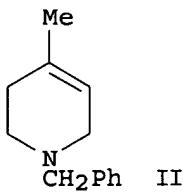
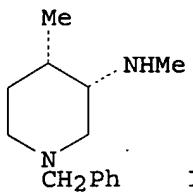
CRN 32634-66-5

CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



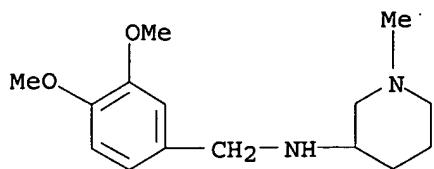
GI



AB Cis-N-benzyl-3-methylamino-4-methylpiperidine I was prepared in >10 kg quantities by a six-step route. Benzylation of 4-methylpyridine followed by reduction with sodium borohydride in ethanol provided methylbenzyltetrahydropyridine II in good yield and purity. Complexation of II with boron trifluoride etherate followed by hydroboration with borane-THF complex, oxidation, and workup provided the piperidinol III as the major isomer; oxidation to the ketone and reductive amination with methylamine and sodium triacetoxyborohydride then provided I'. I was resolved with p-toluoyl-L-tartaric acid to provide nonracemic I in 99.2% ee. The hydroboration-oxidation and reductive amination reactions and their workups were optimized carefully. Alternative routes to I were studied.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1961:144163 CAPLUS
 DOCUMENT NUMBER: 55:144163
 ORIGINAL REFERENCE NO.: 55:27301h-i,27302a-i,27303a-f
 TITLE: Application of sodium borohydride
 reduction to synthesis of
 substituted aminopiperidines, aminopiperazines,
 aminopyridines, and hydrazines
 AUTHOR(S): Walker, Gordon N.; Moore, Miriam Ann; Weaver, Barbara
 N.
 CORPORATE SOURCE: Ciba Pharm. Prods. Inc., Summit, NJ
 SOURCE: Journal of Organic Chemistry (1961), 26, 2740-7
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 55:144163
 IT 132467-51-7, Piperidine, 1-methyl-3-veratrylamino-,
 dihydrochlorides
 (preparation of)
 RN 132467-51-7 CAPLUS
 CN Piperidine, 1-methyl-3-veratrylamino-, dihydrochloride (6CI) (CA INDEX
 NAME)



● 2 HCl

AB Quaternization of 4-aminopyridine (I) with alkyl and arylalkyl halides gave 4-aminopyridinium salts, which were reduced with NaBH₄ to 1-(alkyl or arylalkyl)-4-aminopiperidines. Both 1-alkyl-4-aminopiperidines and 1-alkyl-4-aminopiperazines could be converted to Schiff bases, which were reduced with NaBH₄ to the corresponding secondary amines. Similar reduction of appropriate Schiff bases as a means of preparing substituted 3-aminopiperidines, aminopyridines, and aminomethylpyridines, as well as reduction of dialkylhydrazones to the corresponding trisubstituted hydrazines were also described. Anhydrous HBr was passed through a cold solution of 33.6 g. veratryl alc. in 500 ml. C₆H₆ 10 min., the lower layer separated, the C₆H₆ treated with Na₂CO₃, stirred, the solution of veratryl bromide (II) filtered, and used in the following step without purification. To the C₆H₆ solution of II was added 19 g. I; the mixture refluxed 1.5 hrs., filtered, and the product crystallized gave 54 g. 1-(3,4-dimethoxybenzyl)-4-aminopyridinium bromide (IIa), m. 248-50° (decomposition), (alc.). A simple two-step synthesis was used in the preparation of the 1,2-diphenylethyl- and 3,4-dimethoxyphenacyl-substituted compds. The remaining substances were prepared from the com. available bromo (in one case, iodo) compds. by the same procedure with a few modifications in solvents used and reaction times. In reactions involving α,ω-dibromoalkanes, a mixture of the compound, 2 equivs. I, and a suitable amount of PhMe was refluxed. The product often settled as an oil. In this case the supernatant was decanted, and the oil crystallized 2-Methyl-4-aminopyridine (III) was most conveniently synthesized by a 2-step reduction of 4-nitro-2-picoline N-oxide as follows. (A) The oxide (45 g.) in 200 ml. alc. containing 4 g. 10% Pd-C shaken under H at 45 lb./sq. in. gave 33 g. 2-methyl-4-aminopyridine N-oxide (IV), yellow crystals, m. 181-3° (alc.). IV (30 g.) in 300 ml. 1:1 AcOH-H₂O treated with excess Zn dust, the mixture warmed 1 hr., cooled, covered with Et₂O, treated with a 40% solution of 500 g. NaOH, and the Et₂O solution evaporated gave 16.8 g. III, m. 95° (cyclohexane). The following (4-H₂NC₅H₄N)RBr were obtained (R, solvent prepared in, reflux time in hrs., % yield, and m.p. given): EtO₂CCH₂, C₆H₆-alc., 1.5, 92, 197°; EtO₂CCH₂CH₂, PhMe, 5, 73, 159°; HOCH₂CH₂, PhMe, 3.5, 80, 131°; PhCH₂, C₆H₆, 0.5, 90, 196°; Ph₂CH, PhMe, 3, 56, 263°; PhCH₂CH₂, PhMe, 2, 77, 260°; PhCH₂CHPh, C₆H₆, 9, 53, 245°; PhOCH₂CH₂, PhMe, 4.5, 75, 184°; BzCH₂, C₆H₆, 2, 96, 308°; 3,4-(MeO)₂C₆H₃COCH₂, C₆H₆-alc., 0.3, 64, 271°; p-O₂NC₆H₄CH₂, PhMe, 5.5, 66, 266°; 2,4-(O₂N)C₆H₃, PhMe, 1, 56, 294°. The following [4-H₂NC₅H₄N(CH₂)_nNC₅H₄-4]Br₂ were similarly obtained (n, solvent, reflux time, % yield, and m.p. of product given): 4, PhMe, 2, 87, 273°; 6, PhMe, 14, 91, 303°; 8, PhMe, 5.5, 84, 300°; 9, PhMe, 5, 14, 221°; 10, PhMe, 5, 88, 247°; 11, PhMe, 7.5, 48, 216°; 12, PhMe, 13, 29, 209°; 16, PhMe (prepared from alkyl iodide), 11, 94, 185°. The following

[2, 4-Me(H₂N)C₅H₄N(CH₂)nNC₅H₄(NH₂)Me- 4, 2]Br₂ were obtained (n, solvent, reflux time in hrs., % yield, and m.p. given): 8, PhMe, 8, 60, 304°; 9, PhMe, 9, 17, 275°. IIa (30 g.) in 700 ml. MeOH treated in 1 hr. with 250 g. NaBH₄, the mixture heated on a steam bath, cooled, treated with 500 ml. H₂O, covered with 2 l. Et₂O, the 2 phases separated, evaporated, the 20 g. oil dissolved in 30 ml. alc., and treated with dry HCl gave 12.2 g. 1-(3,4-dimethoxybenzyl)-4-aminopiperidine-2HCl, m. 223-5° (decomposition) (MeOH-Et₂O). Other 4-aminopiperidines were obtained from the resp. quaternary salts by the same procedure. The free bases were hygroscopic oils. The amines had to be salted out with NaCl. When 4-aminopiperidines, as free bases, were required for further work, they were used directly in the crude state.

1-Methyl-4-aminopiperidine and 1-(β-hydroxyethyl)-4-aminopiperidine, both formed hygroscopic salts with HCl. The following 4-(N-substituted-amino)piperidine-2HCl were thus obtained (R, % yield, and m.p. given): EtO₂CCH₂, 17, 169°; PhCH₂, 41, 255°; PhCH₂CH₂, 88, 321°; PhCH₂CHPh, 40, 237° (decomposition); PhOCH₂CH₂, 44, 220°; PhCH(OH)CH₂, 90, 248° (decomposition); 3,4-(MeO)₂C₆H₃CH(OH)CH₂, 56, 220° (decomposition); p-O₂NC₆H₄CH₂, 10, 265° (decomposition). The following 4-H₂NC₅H₄N(CH₂)nNC₅H₄NH₂-4·4HCl were similarly obtained (n, % yield, and m.p. given): 6, 22, 204°; 10, 16, 295°; 12, 34, 311°; 16, 20, 315°.

1,10-Bis(4-amino-1-piperidyl)decane was also characterized by preparation of the bis(dichloroacetate)-2HCl, m. 227-30° (decomposition) (alc.).

1-Methyl-4-aminopiperazine (8.1 g.) and 11.2 g. veratraldehyde in 200 ml. PhMe refluxed 1.5 hrs., evaporated, the residue dissolved in 150 ml. MeOH, the solution reduced with 40 g. NaBH₄, heated 0.5 hr. on the steam bath, and the 20.5 g. yellow oil treated with alc. HCl gave 10 g. 1-methyl-4-(3,4-dimethoxybenzylamine)piperazine, m. 199-202° (decomposition). Other secondary aminopiperidines and aminopiperazines were given in a table. Attempts to reduce imines derived from 1-phenyl-2-propanone and 1-substituted 4-aminopiperidines with NaBH₄ did not lead to desired products, probably because of cleavage of the unstable imines.

3-Aminopyridine (16.8 g.) and 30 g. veratraldehyde in 500 ml. xylene refluxed 24 hrs. and the 45.5 g. residual oily imine in MeOH reduced with NaBH₄ gave 33 g. 3-(3,4-dimethoxybenzylamino)pyridino (V), m. 123-5° (MeOH). The other pyridines were similarly prepared. The following RNHR' were thus obtained (R, R', % yield, and m.p. given): 3,4-dimethoxybenzyl, 1-methyl-4-piperidyl, 60, 254-6° (decomposition); 3,4,5-trimethoxybenzyl, 1-methyl-4-piperidyl, 37, 264-5° (decomposition); 3,4-dimethoxybenzyl, 1-(β-hydroxyethyl)-4-piperidyl, 12, 255-6° (decomposition); 4-methoxybenzyl, 1-(3,4-dimethoxybenzyl)-4-piperidyl, 46, 274-5° (decomposition); 3,4,5-trimethoxybenzyl, 1-methyl-4-piperazyl, 56, 135-7°; p-dimethylaminobenzyl, 1-methyl-4-piperazyl, 40, 125-7° (157-60°); 3-pyridylmethyl, 1-methyl-4-piperazyl, 95, 201-2° (220-6° with 0.5H₂O); 1-hydroxy-1-phenyl-2-propyl, 1-methyl-4-piperazyl, 25, 219-21° (decomposition); 3,4-dimethoxybenzyl, 2-pyridyl, 65, 102-3°; 3,4,5-trimethoxybenzyl, 2-pyridyl, 45, 167-8°; p-dimethylaminobenzyl, 2-pyridyl, 52, 125-6°; 3,4,5-trimethoxybenzyl, 3-pyridyl, 63, 109-10°; 3,4,5-trimethoxybenzyl, 3-pyridylmethyl, 90, 205-7°; p-dimethylaminobenzyl, 3-pyridylmethyl, 96, 185-6° (decomposition); 3,4-dimethoxybenzyl, 4-pyridylmethyl, 22, 200° (decomposition); 3,4,5-trimethoxybenzyl, 4-pyridylmethyl, 43, 214-16°; p-dimethylaminobenzyl, 4-pyridylmethyl, 45, 195-6°; 1-phenyl-2-propyl, 3-pyridylmethyl, 55, 205-7°; 1-phenyl-2-propyl, 4-pyridylmethyl, 80, 181-3°; 3,4,5-trimethoxybenzyl, NMe₂, 45, 81-3; p-dimethylaminobenzyl, NMe₂, 7, 158-61° (decomposition); 1-phenyl-2-propyl, NMe₂, 70, 123-5°; 1,2-diphenylethyl, NMe₂, 23,

183-5°; PhCH:CHCHMe, NMe₂, 5, 117-20° (decomposition). V (14.1 g.) converted rapidly to the MeI salt, evaporated, the crystals suspended in 200 ml. MeOH, reduced with 125 g. NaBH₄, and the residual oil treated with HCl gave 14.6 g. 1-methyl-3-(3,4-dimethoxybenzylamino)piperidine-2HCl, m. 233-5° (decomposition). 3-Aminopiperidine (7.6 g.), 12.7 g. veratraldehyde, and 250 ml. PhMe refluxed 3.5 hrs., the crude imine reduced with NaBH₄ in alc., and crystallized gave 20.6 g. V.2HCl, m. 229-31° (alc.). Reduction of p-dimethylaminobenzylidene derivative and isolation gave 76% 3-(4-dimethylaminobenzylamino)piperidine, no definite m.p. 3-(3-Pyridylmethylamino)piperidine was obtained in 79% yield by reduction of the 3-pyridylidene derivative and isolated as the tri-HCl salt. Veratraldehyde (16.3 g.) and 6.5 g. N,N-dimethylhydrazine mixed, the oil taken up in 200 ml. C₆H₆, the solution refluxed 4 hrs., evaporated, and the hydrazone reduced in MeOH with NaBH₄ gave 13.9 g. N,N-dimethyl-N-(3,4-dimethoxybenzyl)hydrazine-HCl, m. 172-4.5°. The other hydrazine derivs. above were prepared by the same method

=> d his

(FILE 'HOME' ENTERED AT 12:07:55 ON 06 SEP 2005)

FILE 'REGISTRY' ENTERED AT 12:08:02 ON 06 SEP 2005

L1 STRUCTURE UPLOADED
L2 50 S L1
L3 6103 S L1 FUL

FILE 'CAPLUS' ENTERED AT 12:08:40 ON 06 SEP 2005

L4 1211 S L3
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L7 68 S L5 AND (REDUCING OR REDUCE OR REDUCTION)
L8 4 S L7 AND (BOROHYDRIDE OR LITHIUM ALUMINUM)

=> d 17 ibib hitstr abs 1-68

L7 ANSWER 4 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:433796 CAPLUS
DOCUMENT NUMBER: 141:7031
TITLE: A preparation of 3-amino-piperidine derivatives,
 useful as inhibitors of Janus kinase 3
INVENTOR(S): Ripin, David H. B.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp.
 CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2004102627 | A1 | 20040527 | US 2003-717958 | 20031120 |
| CA 2506016 | AA | 20040603 | CA 2003-2506016 | 20031110 |
| WO 2004046112 | A2 | 20040603 | WO 2003-IB5151 | 20031110 |
| WO 2004046112 | A3 | 20040805 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,

10/717,958

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-428324P P 20021121
WO 2003-IB5151 W 20031110

OTHER SOURCE(S): MARPAT 141:7031

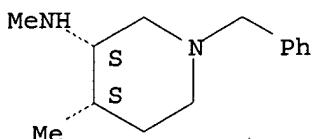
IT 694495-62-0P

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); USES (Uses)
(preparation of aminopiperidine derivs. useful as inhibitors of Janus kinase
3)

RN 694495-62-0 CAPLUS

CN 3-Piperidinamine, N,4-dimethyl-1-(phenylmethyl)-, monohydrochloride,
(3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

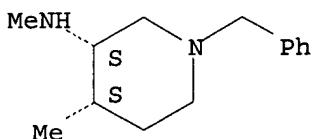
IT 477600-69-4P 694495-65-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of aminopiperidine derivs. useful as inhibitors of Janus kinase
3)

RN 477600-69-4 CAPLUS

CN 3-Piperidinamine, N,4-dimethyl-1-(phenylmethyl)-, (3R,4R)-rel- (9CI) (CA
INDEX NAME)

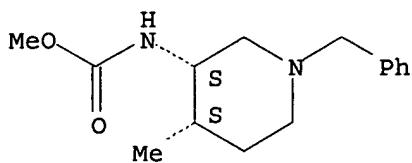
Relative stereochemistry.



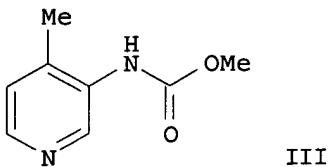
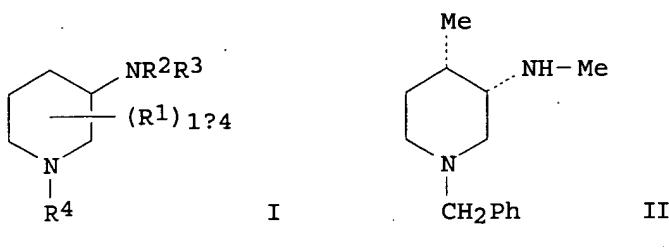
RN 694495-65-3 CAPLUS

CN Carbamic acid, [(3R,4R)-4-methyl-1-(phenylmethyl)-3-piperidinyl]-, methyl
ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



GI



AB The invention relates to a preparation of 3-aminopiperidine derivs. of formula I [wherein: R¹ is carboxy, cyano, deuterium, alkyl, alkoxy, acyl, or alkylamino, etc.; R² is H, alkyl, alkylsulfonyl, or alk(en/yn)yl, etc.; R³ is H, (cyclo)alkyl, (un)substituted alk(en/yn)yl; R⁴ is CO₂R⁵ or CH₂R⁶; R⁵ is (cyclo)alkyl, (un)substituted alk(en/yn)yl; R⁶ is alk(en/yn)yl, (hetero)aryl, or carboalkoxy, etc.], useful as inhibitors of Janus kinase 3. The prepared compds. were screened for JAK3 inhibition and inhibition of human IL-2 dependent T-cell blast proliferation (no biol. data). For instance, piperidine derivative II•HCl was prepared via N-carboxylation of the amine-group of 4-methyl-3-aminopyridine by Me₂CO₃, stereoselective pyridine-ring hydrogenation of the obtained carbamate III, N-benzylation of the piperidine ring, reduction, and subsequent hydrochlorination (example 1).

L7 ANSWER 5 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:182836 CAPLUS

DOCUMENT NUMBER: 140:235711

TITLE: Preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase

INVENTOR(S): Barsanti, Paul A.; Bussiere, Dirksen; Harrison, Stephen D.; Heise, Carla C.; Jansen, Johanna M.; Jazan, Elisa; Machajewski, Timothy D.; McBride, Christopher; McCrea, William R.; Ng, Simon; Ni, Zhi-Jie; Pecchi, Sabina; Pfister, Keith; Ramurthy, Savithri; Renhowe, Paul A.; Shafer, Cynthia M.; Silver, Joel B.; Wagman, Allan; Weismann, Marion

10/717,958

PATENT ASSIGNEE(S) : Chiron Corporation, USA
SOURCE: PCT Int. Appl., 570 pp.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004018419 | A2 | 20040304 | WO 2003-US25990 | 20030819 |
| WO 2004018419 | A3 | 20040603 | | |
| WO 2004018419 | B1 | 20040729 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2496164 | AA | 20040304 | CA 2003-2496164 | 20030819 |
| US 2004092535 | A1 | 20040513 | US 2003-644055 | 20030819 |
| EP 1539754 | A2 | 20050615 | EP 2003-781286 | 20030819 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003013743 | A | 20050705 | BR 2003-13743 | 20030819 |
| PRIORITY APPLN. INFO.: | | | US 2002-405729P | P 20020823 |
| | | | US 2002-426107P | P 20021113 |
| | | | US 2002-426226P | P 20021113 |
| | | | US 2002-426282P | P 20021113 |
| | | | US 2002-428210P | P 20021121 |
| | | | US 2003-460327P | P 20030403 |
| | | | US 2003-460328P | P 20030403 |
| | | | US 2003-460493P | P 20030403 |
| | | | US 2003-478916P | P 20030616 |
| | | | US 2003-484048P | P 20030701 |
| | | | WO 2003-US25990 | W 20030819 |

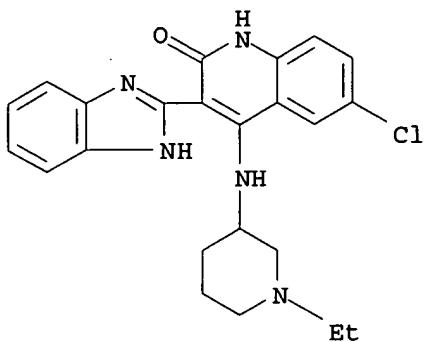
OTHER SOURCE(S) : MARPAT 140:235711

IT 668425-01-2P

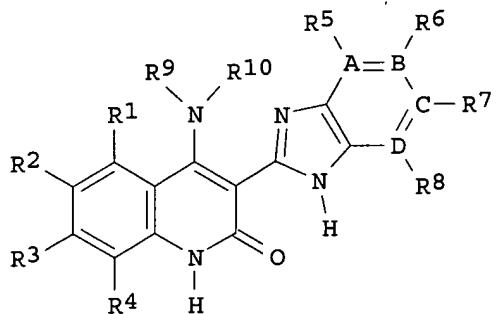
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzimidazole quinolinones for inhibiting a serine/threonine kinase)

RN 668425-01-2 CAPLUS

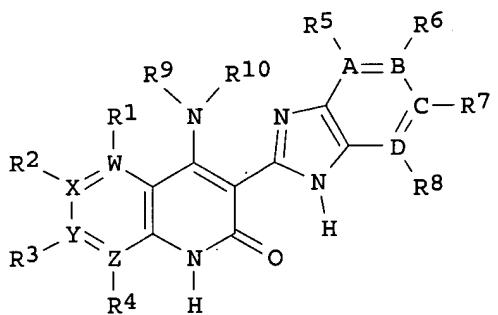
CN 2(1H)-Quinolinone, 3-(1H-benzimidazol-2-yl)-6-chloro-4-[(1-ethyl-3-piperidinyl)amino]- (9CI) (CA INDEX NAME)



GI



I



II

AB The title compds. [I and II; A, B, C, and D = C, N; W, X, Y and Z = C, N and at least one of W, X, Y, and Z = N; R1-R8 = H, halo, CN, NO₂, etc.; R9 = H, (un)substituted alkyl, aryl, etc.; R10 = H; or NR9R10 = 5-7 membered ring], useful for inhibiting various enzymes and treating various conditions, were prepared. E.g., a multi-step synthesis of 4-amino-3-(benzimidazol-2-yl)-6-(4-methylpiperazinyl)hydroquinolin-2-one, was given. The majority of the exemplary compds. I displayed an IC₅₀ of less than 10 μM with respect to VEGFR1, VEGFR2, VEGFR3, FGFR1, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, Cdk4, MEK1, NEK-2, CHK2, CK1ε, Raf, Fyn, Lck, Rsk2, PAR-1, c-Kit, c-ABL, p60src, FGFR3, FLT-3, PDGFRα, and PDGFRβ. In addition, many of the exemplary compds. exhibited IC₅₀ values in the nM range and show potent activity with respect to VEGFR1,

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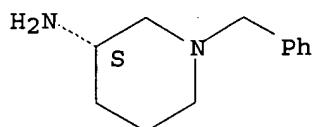
VEGFR2, VEGFR3, FGFR1, FGFR3, c-Kit, c-ABL, FLT-3, CHK1, Cdc2, GSK-3, NEK-2, Cdk2, MEK1, CHK2, Fyn, Lck, Rsk2, PAR-1, PDGFR α , and PDGFR β with IC₅₀ values of less than 1 μ M.

L7 ANSWER 6 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:689660 CAPLUS
DOCUMENT NUMBER: 139:364791
TITLE: Stereocontrolled dopamine receptor binding and subtype selectivity of clebopride analogues synthesized from aspartic acid
AUTHOR(S): Einsiedel, Juergen; Weber, Klaus; Thomas, Christoph; Lehmann, Thomas; Huebner, Harald; Gmeiner, Peter
CORPORATE SOURCE: Emil Fischer Center, Department of Medicinal Chemistry, Friedrich Alexander University, Erlangen, D-91052, Germany
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(19), 3293-3296
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:364791

IT 168466-85-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(acylation of; preparation of benzamide derivs. as clebopride analogs from aspartic acid and their stereocontrolled dopamine receptor binding and subtype selectivity)

RN 168466-85-1 CAPLUS
CN 3-Piperidinamine, 1-(phenylmethyl)-, (3S)- (9CI) (CA INDEX NAME)

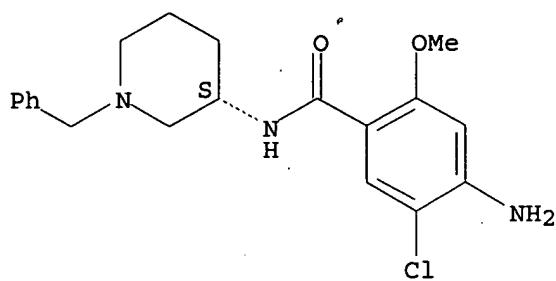
Absolute stereochemistry.



IT 620166-23-6P 620166-25-8P 620166-48-5P
620166-49-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of benzamide derivs. as clebopride analogs from aspartic acid and their stereocontrolled dopamine receptor binding and subtype selectivity)
RN 620166-23-6 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[(3S)-1-(phenylmethyl)-3-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

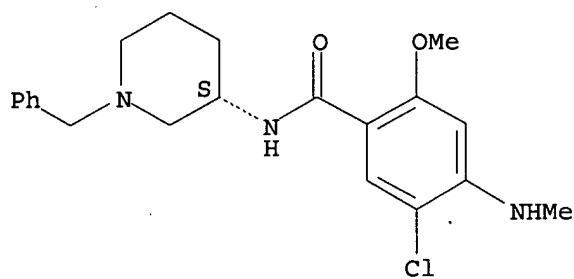
10/717, 958



RN 620166-25-8 CAPLUS

CN Benzamide, 5-chloro-2-methoxy-4-(methylamino)-N-[(3S)-1-(phenylmethyl)-3-piperidinyl]- (9CI) (CA INDEX NAME)

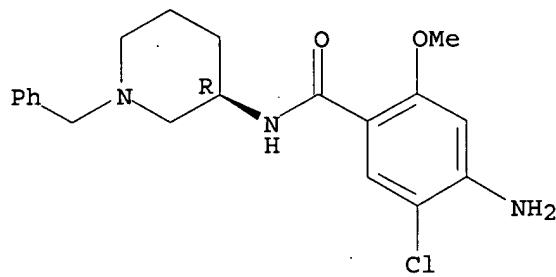
Absolute stereochemistry.



RN 620166-48-5 CAPLUS

CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[(3R)-1-(phenylmethyl)-3-piperidinyl]- (9CI) (CA INDEX NAME)

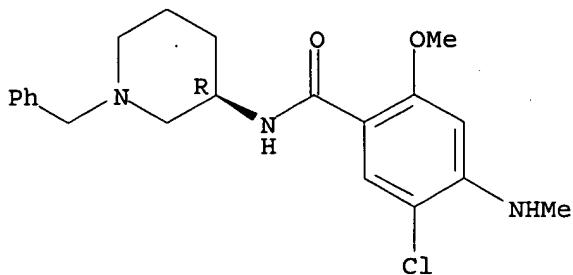
Absolute stereochemistry.



RN 620166-49-6 CAPLUS

CN Benzamide, 5-chloro-2-methoxy-4-(methylamino)-N-[(3R)-1-(phenylmethyl)-3-piperidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



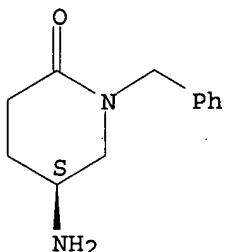
IT 620165-92-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (reduction of; preparation of benzamide derivs. as clebopride analogs from aspartic acid and their stereocontrolled dopamine receptor binding and subtype selectivity)

RN 620165-92-6 CAPLUS

CN 2-Piperidinone, 5-amino-1-(phenylmethyl)-, (5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Employing the achiral 4-aminopiperidine derivative clebopride as a lead compound, chiral analogs were developed displaying dopamine receptor binding profiles that proved to be strongly dependent on the stereochem. Compared to the D1 receptor, the test compds. showed high selectivity for the D2-like subtypes including D2long, D2short, D3 and D4. The highest D4 and D3 affinities were observed for the cis-3-amino-4-methylpyrrolidines and the enantiomer ent3e resulting in Ki values of 0.23 and 1.8 nM, resp. Some benzamides were synthesized in enantiopure form starting from (S)-aspartic acid and its unnatural optical antipode.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:909780 CAPLUS

DOCUMENT NUMBER: 138:137134

TITLE: Development of a Scaleable Route for the Production of cis-N-Benzyl-3-methylamino-4-methylpiperidine

AUTHOR(S): Ripin, David H. Brown; Abele, Stefan; Cai, Weiling; Blumenkopf, Todd; Casavant, Jeffrey M.; Doty, Jonathan L.; Flanagan, Mark; Koecher, Christian; Laue, Klaus W.; McCarthy, Keith; Meltz, Cliff; Munchhoff, Mike; Pouwer, Kees; Shah, Bharat; Sun, Jianmin; Teixeira, John; Vries, Ton; Whipple, David A.; Wilcox, Glenn

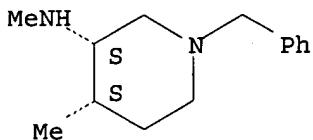
CORPORATE SOURCE: Chemical Research and Development Pfizer Global

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SOURCE: Research Division, Pfizer Inc., Groton, CT, 06340, USA
Organic Process Research & Development (2003), 7(1),
115-120
CODEN: OPRDFK; ISSN: 1083-6160
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:137134

IT 477600-68-3P
RL: IMF (Industrial manufacture); PREP (Preparation)
(large-scale stereoselective preparation of cis-1-benzyl-4-methyl-3-(methylamino)piperidine)
RN 477600-68-3 CAPLUS
CN 3-Piperidinamine, N,4-dimethyl-1-(phenylmethyl)-, dihydrochloride,
(3R,4R)-rel- (9CI) (CA INDEX NAME)

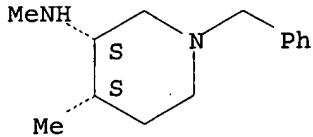
Relative stereochemistry.



● 2 HCl

IT 477600-69-4P
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
(Reactant or reagent)
(large-scale stereoselective preparation of cis-1-benzyl-4-methyl-3-(methylamino)piperidine)
RN 477600-69-4 CAPLUS
CN 3-Piperidinamine, N,4-dimethyl-1-(phenylmethyl)-, (3R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT 493040-24-7P
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation); RACT
(Reactant or reagent)
(resolution in the large-scale stereoselective preparation of nonracemic
cis-1-benzyl-4-methyl-3-(methylamino)piperidine)
RN 493040-24-7 CAPLUS
CN Butanedioic acid, 2,3-bis[(4-methylbenzoyl)oxy]-, (2R,3R)-, compd. with
rel-(3R,4R)-N,4-dimethyl-1-(phenylmethyl)-3-piperidinamine (1:2) (9CI)
(CA INDEX NAME)

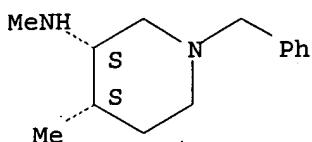
CM 1

CRN 477600-69-4

10/717, 958

CMF C14 H22 N2

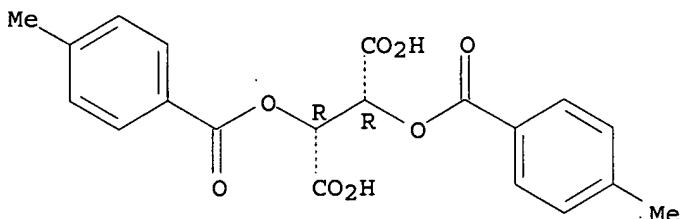
Relative stereochemistry.



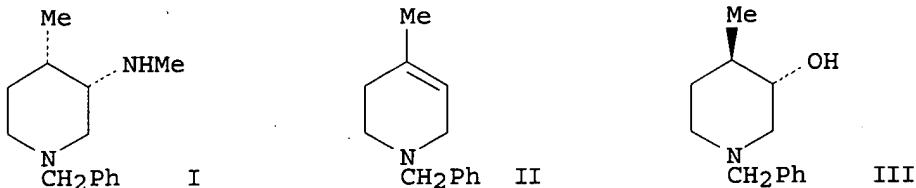
CM 2

CRN 32634-66-5
CMF C20 H18 O8

Absolute stereochemistry. Rotation (-).



GI



AB Cis-N-benzyl-3-methylamino-4-methylpiperidine I was prepared in >10 kg quantities by a six-step route. Benzylation of 4-methylpyridine followed by reduction with sodium borohydride in ethanol provided methylbenzyltetrahydropyridine II in good yield and purity. Complexation of II with boron trifluoride etherate followed by hydroboration with borane-THF complex, oxidation, and workup provided the piperidinol III as the major isomer; oxidation to the ketone and reductive amination with methylamine and sodium triacetoxyborohydride then provided I. I was resolved with p-toluoyl-L-tartaric acid to provide nonracemic I in 99.2% ee. The hydroboration-oxidation and reductive amination reactions and their workups were optimized carefully. Alternative routes to I were studied.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 11 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

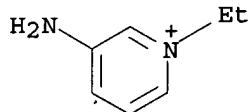
ACCESSION NUMBER: 2002:301818 CAPLUS

DOCUMENT NUMBER: 136:327130

10/717, 958

TITLE: Waterborne color ink sets for ink-jet printing and method for their use
INVENTOR(S): Horinouchi, Kyoko; Suzuki, Atsushi; Hashimoto, Takeshi
PATENT ASSIGNEE(S): Fuji Xerox Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|--|----------|-----------------|----------|
| JP 2002121434 | A2 | 20020423 | JP 2000-312311 | 20001012 |
| PRIORITY APPLN. INFO.: JP 2000-312311 20001012 | | | | |
| IT 179912-77-7 | 3-Amino-N-ethylpyridinium bromide
RL: MOA (Modifier or additive use); USES (Uses)
(surface modifiers; waterborne color ink sets for ink-jet printing and method for use) | | | |
| RN 179912-77-7 | CAPLUS | | | |
| CN Pyridinium, 3-amino-1-ethyl-, bromide (9CI) | (CA INDEX NAME) | | | |



● Br-

AB The inks sets comprise a black ink and at least a cyan ink, a magenta ink and a yellow ink where the black and color inks contain self-dispersible pigments having dispersed particles with volume-average diameter (Dv) 20-150 nm, and Dv/Dn (Dn = the number-average particle diameter) of 1.5-3.0:1 and surface tension 25-55 mN/m and 25-45 mN/m for black ink and color inks, resp., for improving storage and ejection stability and reducing color smear.

L7 ANSWER 15 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:50636 CAPLUS
DOCUMENT NUMBER: 134:115797
TITLE: Synthesis and GlcCer synthase inhibition of amino ceramide-like compounds
INVENTOR(S): Shayman, James A.; Radin, Norman S.
PATENT ASSIGNEE(S): Regents of the University of Michigan, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

| | | | | |
|--|----|----------|-----------------|-------------|
| WO 2001004108 | A1 | 20010118 | WO 2000-US18935 | 20000707 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2378600 | AA | 20010118 | CA 2000-2378600 | 20000707 |
| EP 1196406 | A1 | 20020417 | EP 2000-945332 | 20000707 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| BR 2000012318 | A | 20020528 | BR 2000-12318 | 20000707 |
| JP 2003521479 | T2 | 20030715 | JP 2001-509718 | 20000707 |
| AU 774960 | B2 | 20040715 | AU 2000-59296 | 20000707 |
| US 6890949 | B1 | 20050510 | US 2001-30963 | 20000707 |
| PRIORITY APPLN. INFO.: | | | US 1999-350678 | A1 19990709 |
| | | | US 1999-350768 | A 19990709 |
| | | | WO 2000-US18935 | W 20000707 |

OTHER SOURCE(S): MARPAT 134:115797

IT 189164-46-3P

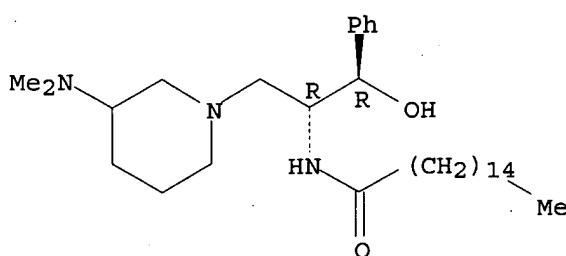
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and GlcCer synthase inhibition of amino ceramide-like compds.)

RN 189164-46-3 CAPLUS

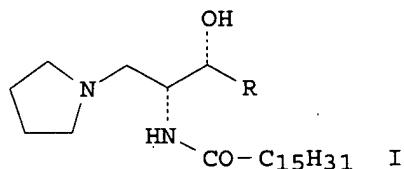
CN Hexadecanamide, N-[(1R,2R)-1-[[3-(dimethylamino)-1-piperidinyl]methyl]-2-hydroxy-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Currently available stereo shown.



GI



AB Synthesis of amino ceramide-like compds. (I) (R = 3,4-ethylenedioxyphenyl, 4-hydroxyphenyl) are disclosed which inhibit

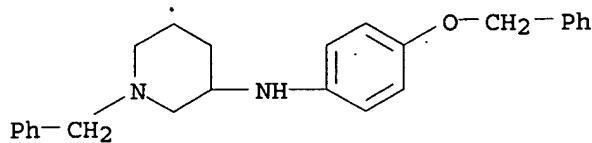
glucosyl ceramide (GlcCer) formation by inhibiting the enzyme GlcCer synthase, thereby lowering the level of glycosphingolipids. Thus, I (R = 4-HOC₆H₄) (II) is prepared from 4-hydroxyacetophenone by hydroxy protection with benzyl bromide followed by bromination of acetyl, amination of bromide, amidation with palmitoyl chloride, condensation with formaldehyde and pyrrolidine, ketone reduction, debenzylation and resolution with chiral chromatog. II shows an IC₅₀ of 0.5 in GlcCer synthase inhibition assay. The compds. of the present invention have improved GlcCer synthase inhibition activity and are therefore highly useful in therapeutic methods for treating various conditions and diseases associated with altered glycosphingolipid levels.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

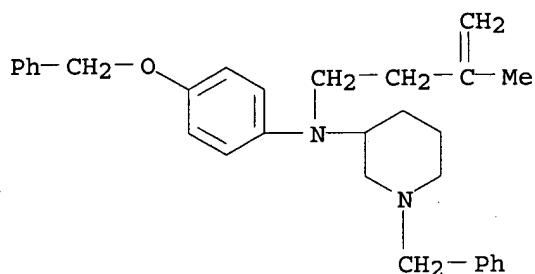
L7 ANSWER 20 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1999:126886 CAPLUS
 DOCUMENT NUMBER: 130:196584
 TITLE: Preparation of aniline derivatives as calcium channel blockers
 INVENTOR(S): Hu, Lain-Yen; Rafferty, Michael Francis; Ryder, Todd Robert
 PATENT ASSIGNEE(S): Warner-Lambert Company, USA
 SOURCE: PCT Int. Appl., 137 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|-------------|
| WO 9907689 | A1 | 19990218 | WO 1998-US15907 | 19980729 |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IS,
JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG,
SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD,
RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9887627 | A1 | 19990301 | AU 1998-87627 | 19980729 |
| ZA 9807144 | A | 19990510 | ZA 1998-7144 | 19980807 |
| US 6251918 | B1 | 20010626 | US 1999-402196 | 19990929 |
| US 2001023249 | A1 | 20010920 | US 2001-769798 | 20010125 |
| US 6495715 | B2 | 20021217 | | |
| US 2003060632 | A1 | 20030327 | US 2002-252854 | 20020923 |
| PRIORITY APPLN. INFO.: | | | US 1997-55251P | P 19970811 |
| | | | US 1998-82358P | P 19980420 |
| | | | WO 1998-US15907 | W 19980729 |
| | | | US 1999-402196 | A3 19990929 |
| | | | US 2001-769798 | A3 20010125 |

OTHER SOURCE(S): MARPAT 130:196584
 IT 220741-70-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (N-alkenylation; preparation of aniline derivs. as calcium channel blockers)
 RN 220741-70-8 CAPLUS
 CN 3-Piperidinamine, N-[4-(phenylmethoxy)phenyl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)

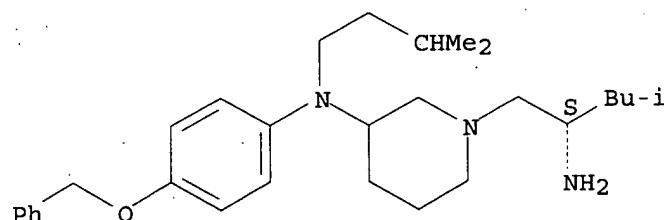


IT 220741-71-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (debenzylation; preparation of aniline derivs. as calcium channel blockers)
 RN 220741-71-9 CAPLUS
 CN 3-Piperidinamine, N-(3-methyl-3-butenyl)-N-[4-(phenylmethoxy)phenyl]-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



IT 220739-46-8P 220739-48-0P 220739-50-4P
 220739-53-7P 220739-55-9P 220739-57-1P
 220739-59-3P 220739-61-7P 220739-64-0P
 220739-65-1P 220739-67-3P 220739-72-0P
 220739-76-4P 220739-80-0P 220739-83-3P
 220739-87-7P 220739-91-3P 220740-41-0P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of aniline derivs. as calcium channel blockers)
 RN 220739-46-8 CAPLUS
 CN 1-Piperidineethanamine, 3-[(3-methylbutyl)[4-(phenylmethoxy)phenyl]amino]-
 α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

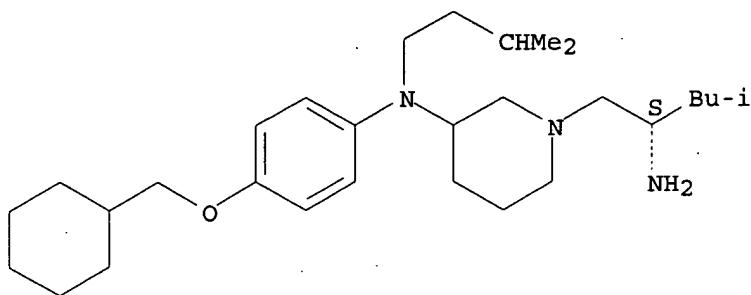
Absolute stereochemistry.



RN 220739-48-0 CAPLUS
 CN 1-Piperidineethanamine, 3-[[4-(cyclohexylmethoxy)phenyl](3-methylbutyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

10/717, 958

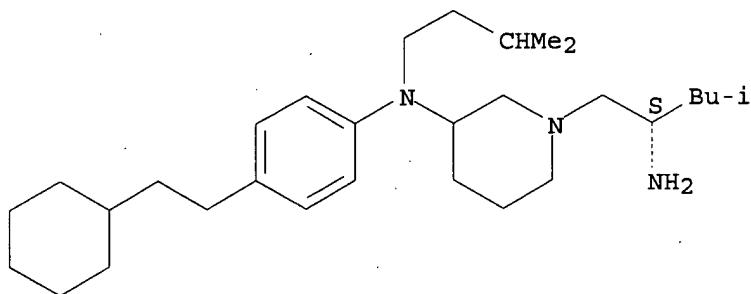
Absolute stereochemistry.



RN 220739-50-4 CAPLUS

CN 1-Piperidineethanamine, 3-[(4-(2-cyclohexylethyl)phenyl](3-methylbutyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

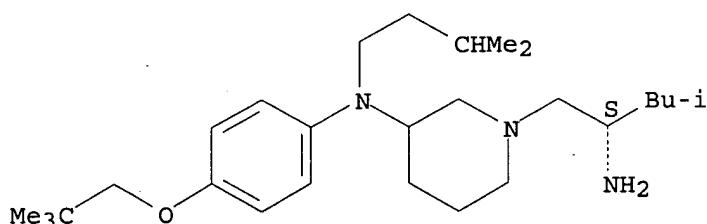
Absolute stereochemistry.



RN 220739-53-7 CAPLUS

CN 1-Piperidineethanamine, 3-[(4-(2,2-dimethylpropoxy)phenyl](3-methylbutyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

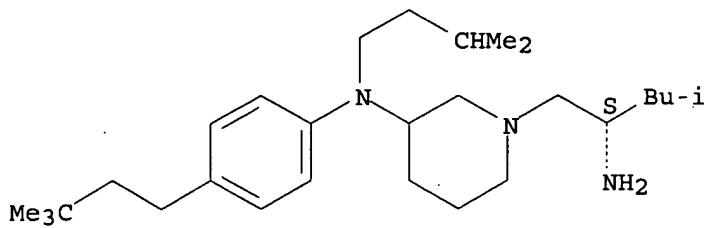
Absolute stereochemistry.



RN 220739-55-9 CAPLUS

CN 1-Piperidineethanamine, 3-[(4-(3,3-dimethylbutyl)phenyl](3-methylbutyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

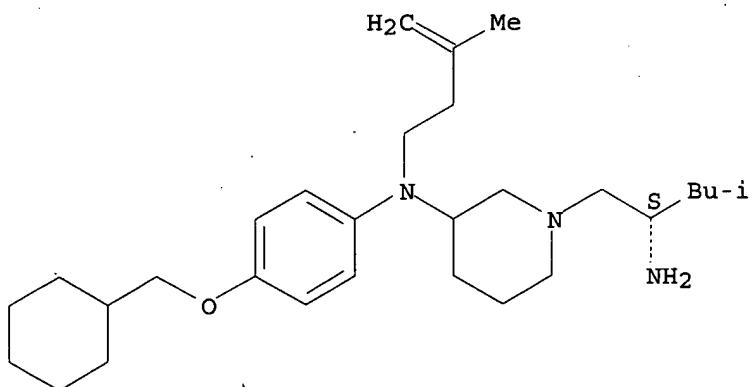
Absolute stereochemistry.



RN 220739-57-1 CAPLUS

CN 1-Piperidineethanamine, 3-[4-(cyclohexylmethoxy)phenyl](3-methyl-3-butenyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

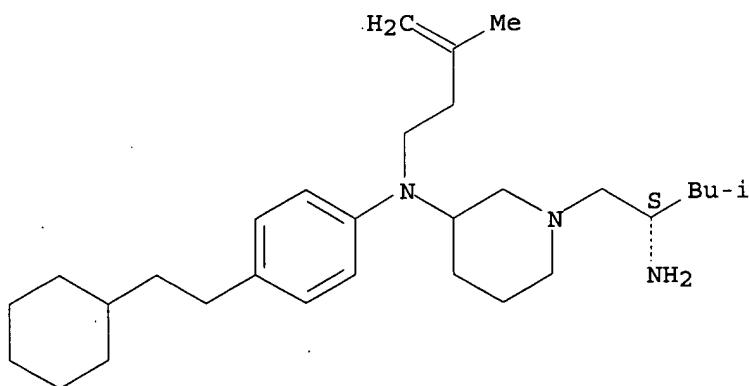
Absolute stereochemistry.



RN 220739-59-3 CAPLUS

CN 1-Piperidineethanamine, 3-[4-(2-cyclohexylethyl)phenyl](3-methyl-3-but enyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



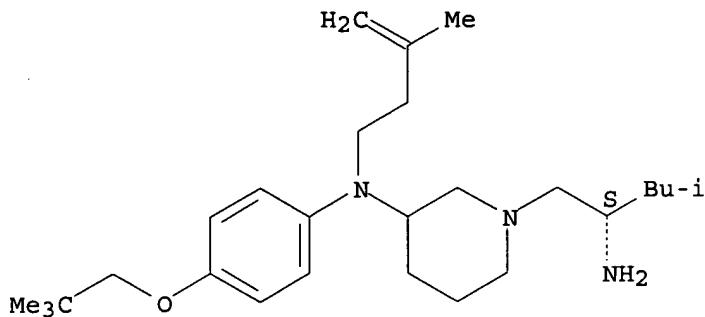
RN 220739-61-7 CAPLUS

CN 1-Piperidineethanamine, 3-[4-(2,2-dimethylpropoxy)phenyl](3-methyl-3-but enyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

10/717, 958

NAME)

Absolute stereochemistry.

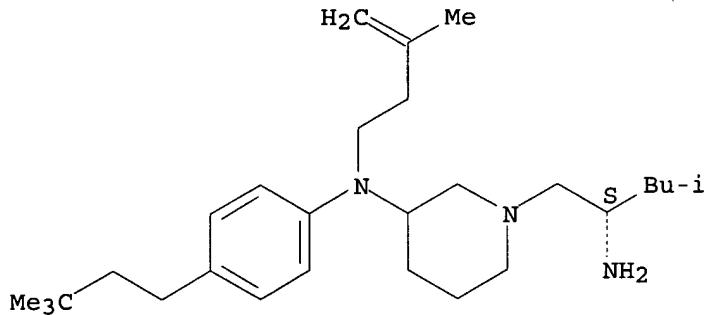


RN 220739-64-0 CAPLUS

CN 1-Piperidineethanamine, 3-[[(4-(3,3-dimethylbutyl)phenyl)(3-methyl-3-but enyl)amino]-alpha-(2-methylpropyl)-, (alphaS)- (9CI) (CA INDEX

NAME)

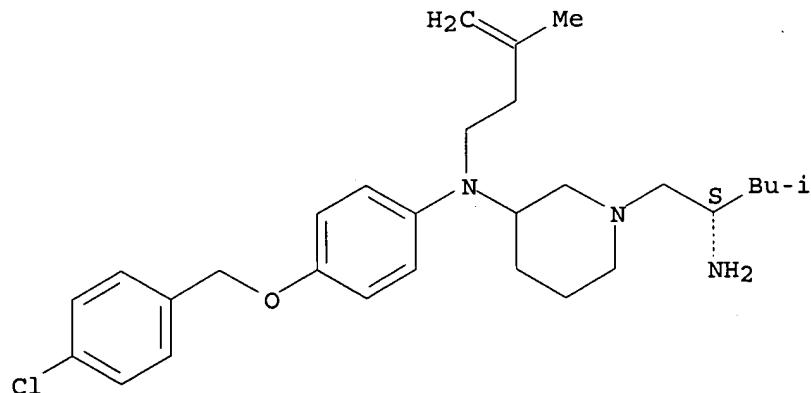
Absolute stereochemistry.



RN 220739-65-1 CAPLUS

CN 1-Piperidineethanamine, 3-[[(4-[(4-chlorophenyl)methoxy]phenyl)(3-methyl-3-but enyl)amino]-alpha-(2-methylpropyl)-, (alphaS)- (9CI) (CA INDEX
NAME)

Absolute stereochemistry.

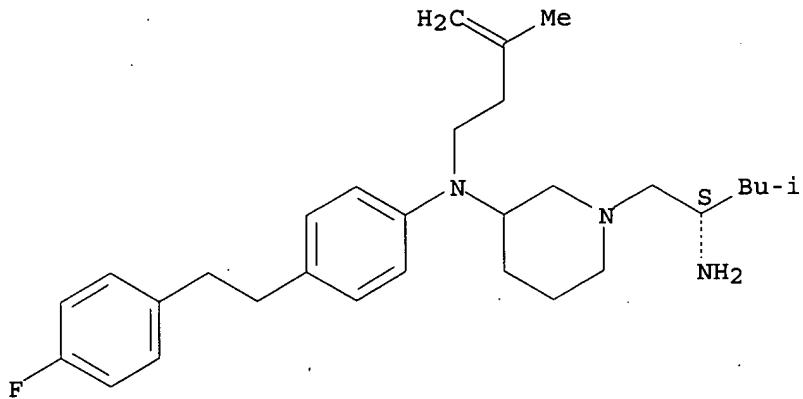


10/717, 958

RN 220739-67-3 CAPLUS

CN 1-Piperidineethanamine, 3-[[4-[2-(4-fluorophenyl)ethyl]phenyl](3-methyl-3-butenyl)amino]- α -(2-methylpropyl)-, (α S)- (9CI) (CA INDEX NAME)

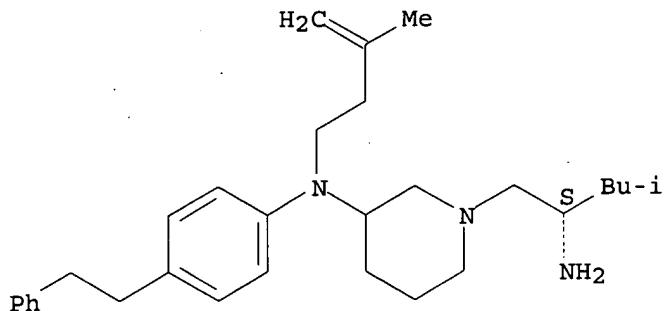
Absolute stereochemistry.



RN 220739-72-0 CAPLUS

CN 1-Piperidineethanamine, 3-[(3-methyl-3-butenyl)[4-(2-phenylethyl)phenyl]amino]- α -(2-methylpropyl)-, (α S)- (9CI) (CA INDEX NAME)

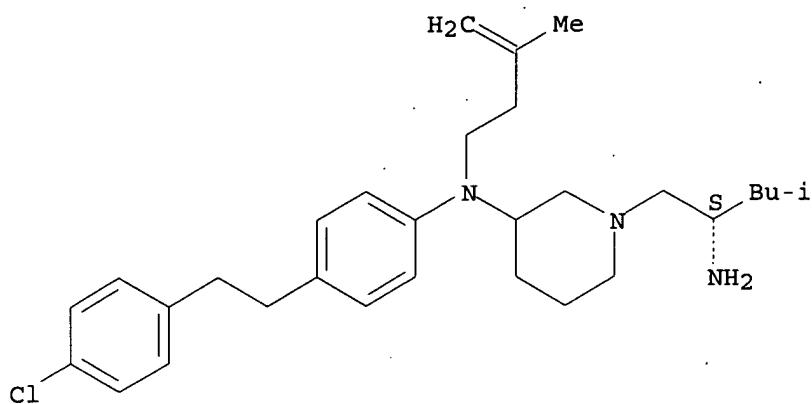
Absolute stereochemistry.



RN 220739-76-4 CAPLUS

CN 1-Piperidineethanamine, 3-[[4-[2-(4-chlorophenyl)ethyl]phenyl](3-methyl-3-butenyl)amino]- α -(2-methylpropyl)-, (α S)- (9CI) (CA INDEX NAME)

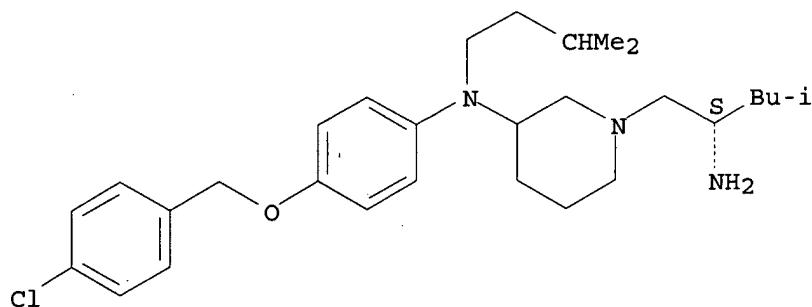
Absolute stereochemistry.



RN 220739-80-0 CAPLUS

CN 1-Piperidineethanamine, 3-[[4-[(4-chlorophenyl)methoxy]phenyl](3-methylbutyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

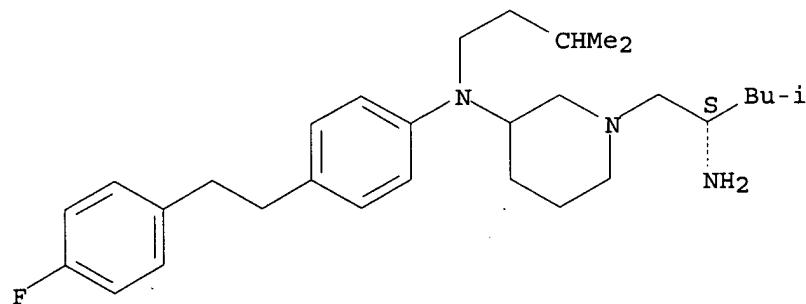
Absolute stereochemistry.



RN 220739-83-3 CAPLUS

CN 1-Piperidineethanamine, 3-[[4-[(2-(4-fluorophenyl)ethyl)phenyl](3-methylbutyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

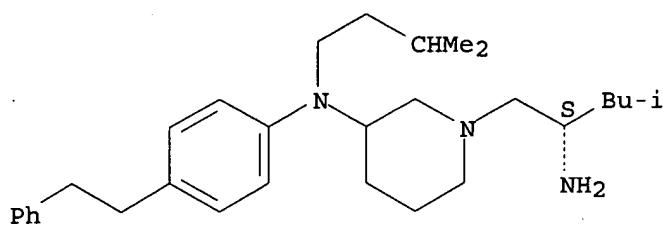


RN 220739-87-7 CAPLUS

CN 1-Piperidineethanamine, 3-[(3-methylbutyl)[4-(2-phenylethyl)phenyl]amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

10/717, 958

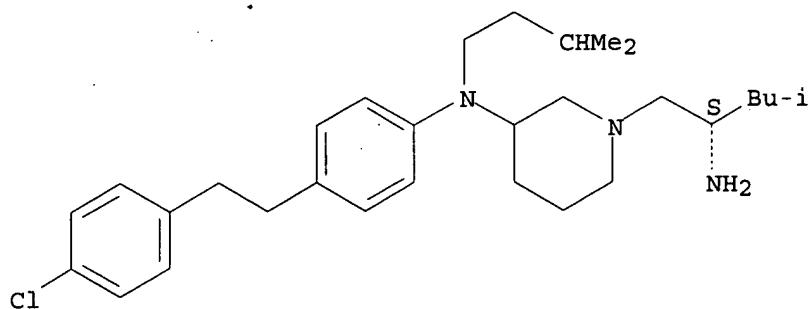
Absolute stereochemistry.



RN 220739-91-3 CAPLUS

CN 1-Piperidineethanamine, 3-[[4-[2-(4-chlorophenyl)ethyl]phenyl](3-methylbutyl)amino]-α-(2-methylpropyl)-, (αS)- (9CI) (CA INDEX NAME)

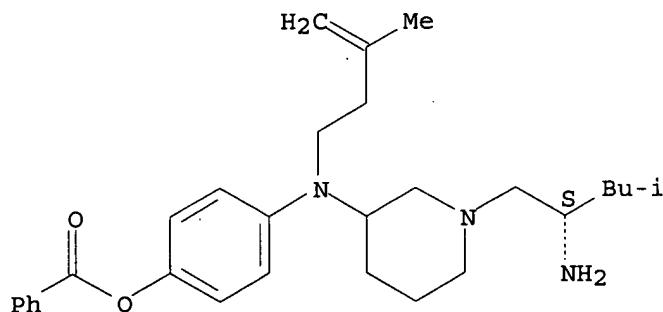
Absolute stereochemistry.



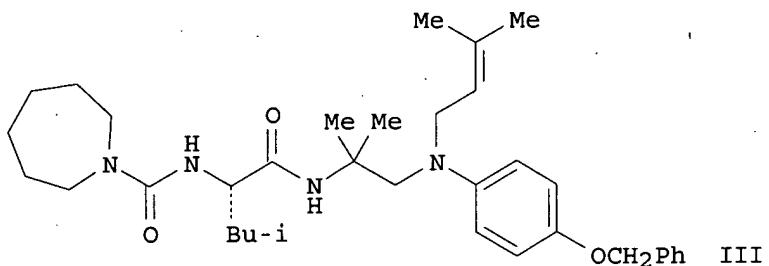
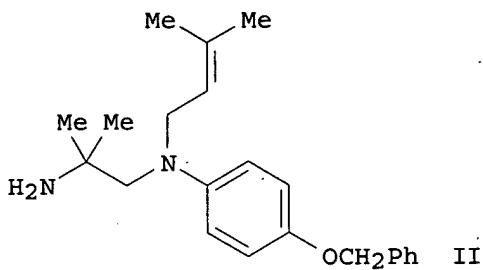
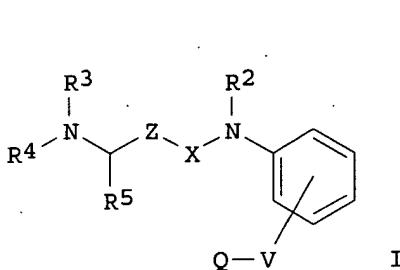
RN 220740-41-0 CAPLUS

CN Phenol, 4-[[1-[(2S)-2-amino-4-methylpentyl]-3-piperidinyl](3-methyl-3-but enyl)amino]-, benzoate (ester) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



AB The invention provides compds. that block calcium channels. In particular, the invention claims compds. I [Z = CH₂ or CO; X = cycloalkylene, (un)substituted heterocycloalkylene, imino or iminoalkylene, certain piperidinediyl or pyrrolidinediyl radicals or their alkylene derivs.; Q = H, (un)substituted aryl, heteroaryl, cycloalkyl, alkyl, heterocycloalkyl; V = O(CH₂)_n or (CH₂)_nO, O, (CH₂)_n, CH:CH, NH(CH₂)_n or (CH₂)_nNH or derivs.; R₂ = H, alkenyl, cycloalkenyl, (un)substituted Ph, alkyl, cycloalkyl, or Ph; R₃ = H, alkyl, alkenyl; R₄ = H, cyclo-(CH₂)_mNCO, alkyl, alkenyl, (un)substituted Ph, heteroaryl, or cycloalkyl; or NR₃R₄ = 5- to 7-membered ring with an optional addnl. heteroatom; R₅ = alkyl, (un)substituted Ph or heteroaryl; m = 1-3; n = 0-3] and their pharmaceutically acceptable salts, esters, amides, and prodrugs. The invention also provides methods of using the compds. to treat stroke, cerebral ischemia, head trauma, or epilepsy, and to pharmaceutical compns. that contain the compds. Over 50 synthetic examples are given, and these plus a large number of addnl. invention compds. are specifically claimed. For instance, N-BOC- α -aminoisobutyric acid underwent amidation with 4-benzyloxyaniline, followed by redn. of the amide with diborane, N-alkenylation with 4-bromo-2-methyl-2-butene, and acidic deprotection to remove BOC, to give intermediate II. In a sep. preparation, H-Leu-OCH₂Ph was treated with triphosgene and hexamethylenamine, then deprotected, to give Hac-Leu-OH (III; Hac = hexamethylenaminocarbonyl). Coupling of II with III using HBTU and DIPEA in DMF gave title compound IV. The latter blocked calcium flux through N-type Ca²⁺ channels in IMR-32 neuronal tumor cells in vitro, with IC₅₀ of 0.26 μ M. Selected compds. gave 20-100% protection of mice from tonic seizures in a sound chamber, at doses of 10-30 mg/kg i.v.

REFERENCE COUNT: . 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:321421 CAPLUS

DOCUMENT NUMBER: 126:288113

TITLE: Aminoceramide-like compounds and therapeutic

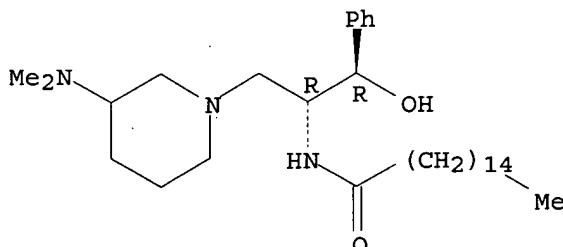
methods of use

INVENTOR(S) : Shayman, James A.; Radin, Norman S.
 PATENT ASSIGNEE(S) : Regents of the University of Michigan, USA
 SOURCE: PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 9710817 | A1 | 19970327 | WO 1996-US14219 | 19960905 |
| W: CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| PRIORITY APPLN. INFO.: | | | US 1995-4047P | P 19950920 |
| OTHER SOURCE(S): MARPAT 126:288113 | | | | |
| IT 189164-46-3, BML 121 | | | | |
| RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) | | | | |
| (aminoceramide-like compds. and therapeutic methods of use) | | | | |
| RN 189164-46-3 CAPLUS | | | | |
| CN Hexadecanamide, N-[(1R,2R)-1-[3-(dimethylamino)-1-piperidinyl]methyl]-2-hydroxy-2-phenylethyl]- (9CI) (CA INDEX NAME) | | | | |

Absolute stereochemistry.

Currently available stereo shown.



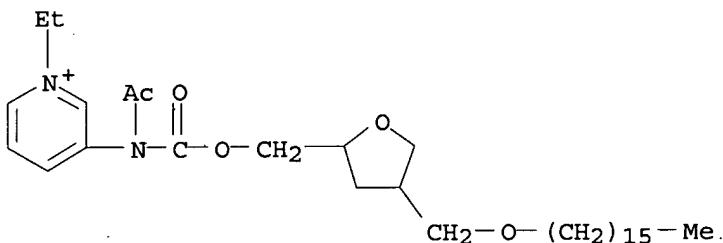
AB Aminoceramide-like compds. are provided which inhibit glucosylceramide (GlcCer) formation by inhibiting the enzyme GlcCer synthase, thereby lowering the level of glycosphingolipids. The compds. of the invention have improved GlcCer synthase inhibition activity and are therefore highly useful in therapeutic methods for treating various conditions and diseases associated with altered glycosphingolipid levels.

L7 ANSWER 34 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:101785 CAPLUS
 DOCUMENT NUMBER: 114:101785
 TITLE: Disubstituted tetrahydrofurans and dioxolanes as platelet activating factor (PAF) antagonists
 AUTHOR(S): Bartroli, Javier; Carceller, Elena; Merlos, Manuel; Garcia-Rafanell, Julian; Forn, Javier
 CORPORATE SOURCE: Chem. Lab., J. Uriach and Cia S. A., Barcelona, 08026, Spain
 SOURCE: Journal of Medicinal Chemistry (1991), 34(1), 373-86
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal

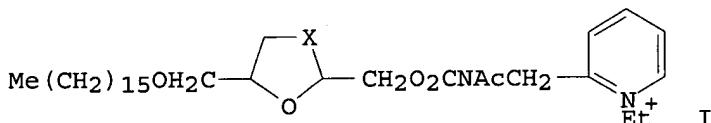
10/717,958

LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:101785
IT 131830-70-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and platelet activating factor antagonist and antihypertensive activity of)
RN 131830-70-1 CAPLUS
CN Pentitol, 1,4-anhydro-2,3-dideoxy-2-[(hexadecyloxy)methyl]-, acetyl(1-ethylpyridinium-3-yl)carbamate, iodide (9CI) (CA INDEX NAME)



● I⁻

GI



AB A new series of disubstituted THF and dioxolane derivs., including I (X = CH₂, O), were prepared by a number of synthetic approaches and evaluated for their PAF antagonist activity in in vitro platelet-aggregation and in vivo hypotension PAF-induced tests. Several of these compds. such as I (X = CH₂) exhibited more potent activity than structurally related 2-[N-acetyl-N-[[[2-methoxy-3-[(octadecylcarbamoyl)oxy]propoxy]carbonyl]amino]methyl]-1-ethylpyridinium chloride (CV-6209) in the in vitro assay, whereas all showed less potency in the in vivo test. The role of both the substituent nature and the placement and number of oxygen atoms in the ring are discussed. A qual. structure activity relationship study was carried out on these nuclei.

L7 ANSWER 35 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:42513 CAPLUS

DOCUMENT NUMBER: 114:42513

TITLE: Synthesis of piperidine derivatives as potential analgesic agents

AUTHOR(S): Jilek, Jiri; Rajsner, Miolsav; Valenta, Vladimir; Borovicka, Milos; Holubek, Jiri; Ryska, Miroslav; Svatek, Emil; Metys, Jan; Protiva, Miroslav

CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 60, Czech.

10/717, 958

SOURCE: Collection of Czechoslovak Chemical Communications
(1990), 55(7), 1828-53
CODEN: CCCCAK; ISSN: 0010-0765

DOCUMENT TYPE: Journal

LANGUAGE: English

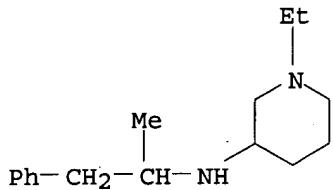
OTHER SOURCE(S): CASREACT 114:42513

IT 130820-17-6P 130820-43-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activities of)

RN 130820-17-6 CAPLUS

CN 3-Piperidinamine, 1-ethyl-N-(1-methyl-2-phenylethyl)- (9CI) (CA INDEX NAME)



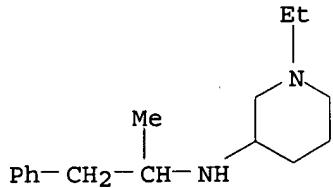
RN 130820-43-8 CAPLUS

CN 3-Piperidinamine, 1-ethyl-N-(1-methyl-2-phenylethyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 130820-17-6

CMF C16 H26 N2

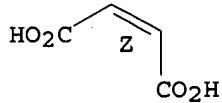


CM 2

CRN 110-16-7

CMF C4 H4 O4

Double bond geometry as shown.



IT 6789-94-2, 3-Amino-1-ethylpiperidine

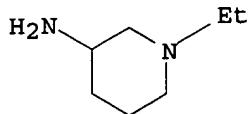
RL: RCT (Reactant); RACT (Reactant or reagent)

10/717, 958

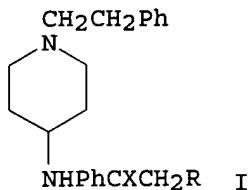
(sequential condensation with phenylacetone and hydride reduction
of)

RN 6789-94-2 CAPLUS

CN 3-Piperidinamine, 1-ethyl- (9CI) (CA INDEX NAME)



GI



AB Forty piperidine derivs. were prepared and tested for analgesic activity. Only the fentanyl analogs I (X = O, R = OMe, SMe; X = S, R = Me) showed strong analgesic activity.

L7 ANSWER 36 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1990:611828 CAPLUS

DOCUMENT NUMBER: 113:211828

TITLE: Preparation of 1-(aminoalkyl)indoles useful as analgesic agents or as intermediates and their production processes

INVENTOR(S): Bell, Malcolm R.

PATENT ASSIGNEE(S): Sterling Drug Inc., USA

SOURCE: Can., 114 pp. Division of Can. Appl. No. 488,073.

CODEN: CAXXA4

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| CA 1258070 | A2 | 19890801 | CA 1988-576124 | 19880830 |
| US 4581354 | A | 19860408 | US 1985-755239 | 19850715 |
| CA 1246563 | A1 | 19881213 | CA 1985-488073 | 19850802 |
| US 4634776 | A | 19870106 | US 1985-810942 | 19851219 |
| US 32761 | E | 19881004 | US 1987-29302 | 19870323 |
| CA 1255305 | A2 | 19890606 | CA 1988-576122 | 19880830 |
| CA 1255316 | A2 | 19890606 | CA 1988-576123 | 19880830 |
| CA 1255312 | A2 | 19890606 | CA 1988-576125 | 19880830 |
| CA 1258069 | A2 | 19890801 | CA 1988-576121 | 19880830 |
| US 4885295 | A | 19891205 | US 1988-255305 | 19881011 |
| FI 8903253 | A | 19890704 | FI 1989-3253 | 19890704 |
| FI 8903254 | A | 19890704 | FI 1989-3254 | 19890704 |
| FI 8903255 | A | 19890704 | FI 1989-3255 | 19890704 |
| FI 8903256 | A | 19890704 | FI 1989-3256 | 19890704 |

10/717,958

| | | | | |
|------------|---|----------|----------------|----------|
| FI 8903257 | A | 19890704 | FI 1989-3257 | 19890704 |
| US 4978664 | A | 19901218 | US 1989-409913 | 19890920 |
| NO 9003304 | A | 19860207 | NO 1990-3304 | 19900725 |
| NO 9003305 | A | 19860207 | NO 1990-3305 | 19900725 |
| NO 9003306 | A | 19860207 | NO 1990-3306 | 19900725 |
| US 5013732 | A | 19910507 | US 1990-559787 | 19900730 |

PRIORITY APPLN. INFO.:

| | | |
|----------------|----|----------|
| US 1984-637931 | A | 19840806 |
| US 1985-755239 | A | 19850715 |
| CA 1985-488073 | A3 | 19850802 |
| FI 1985-2973 | A | 19850801 |
| NO 1985-3066 | A1 | 19850802 |
| US 1985-810942 | A3 | 19851219 |
| US 1986-928335 | A1 | 19861107 |
| US 1988-255305 | A3 | 19881011 |
| US 1989-409913 | A3 | 19890920 |

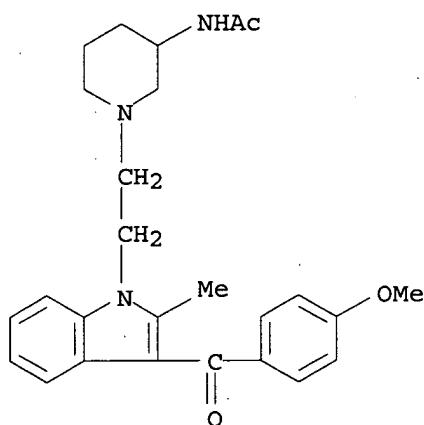
OTHER SOURCE(S): CASREACT 113:211828; MARPAT 113:211828

IT 103610-41-9P 103611-29-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of, as analgesic, antiinflammatory, and antirheumatic)

RN 103610-41-9 CAPLUS

CN Acetamide, N-[1-[2-[3-(4-methoxybenzoyl)-2-methyl-1H-indol-1-yl]ethyl]-3-piperidinyl]- (9CI) (CA INDEX NAME)



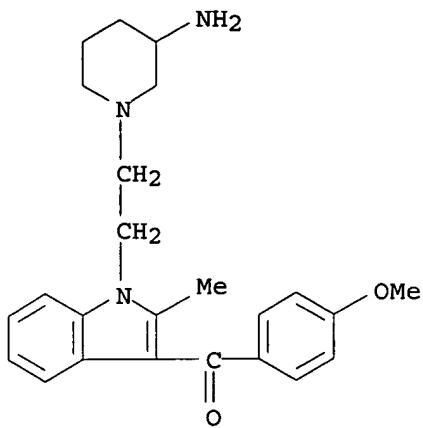
RN 103611-29-6 CAPLUS

CN Methanone, [1-[2-(3-amino-1-piperidinyl)ethyl]-2-methyl-1H-indol-3-yl](4-methoxyphenyl)-, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 103611-28-5

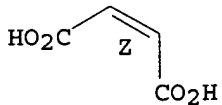
CMF C24 H29 N3 O2



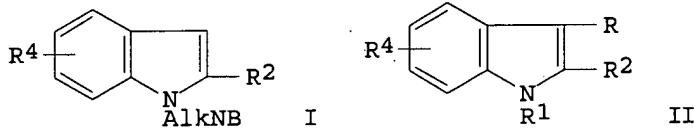
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



GI

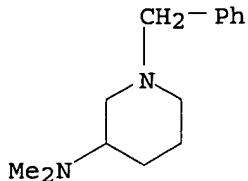


AB Title compds. I [R2 = H, alkyl, Cl, (un)substituted Ph, (un)substituted PhCH2; R4 = H, 1 or 2 substituents such as alkyl, HO, alkoxy, halo in 4-, 5-, 6-, or 7 position; alk = (un)substituted α , ω -alkylene (CH_2) n ; n = 2-6; NB = N3, H2N, alkylamino, hydroxyalkylamino, morpholino, thiomorpholino, piperidino, pyrrolidino, azetidino, pyrrolidino, 1-piperazinyl, hexahydro-4H-1,4-diazepinyl, their oxides, etc.] or an acid addition salt thereof, useful as analgesics (no data) are prepared II (R = R3CZ, R3COCH:CH, R3CO; R3 = cyclohexyl, heterocyclylphenyl, aminomethylphenyl, (un)substituted styryl, biphenyl, (un)substituted naphthyl, heterocyclyl, etc.; CZ = CO, HONC; R1 = H, BNalk, BNCH2CH(OH)CH2] were also prepared and found to possess analgesic, antiinflammatory and antirheumatic activities. II [R = 3-(O2N)C6H4CO; R1 = 2-morpholinoethyl; R2 = Me; R4 = H] in EtOAc and AcOH was reduced with H over Pt oxide to give 83% III [R = 3-(H2N)C6H4CO; R4 = morphoninoethyl; R2 = Me; R1 = H] (III). III, on oral administration, showed an ED50 in acetylcholine-induced abdominal constriction and antibradykinin test of 16 and 53 mg, resp., and on the rat paw flexion test 0.12% at 100 mg/kg.

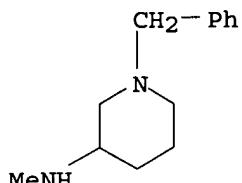
10/717, 958

L7 ANSWER 51 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:582415 CAPLUS
DOCUMENT NUMBER: 85:182415
TITLE: Pharmaceutical compositions and methods of
inhibiting gastric acid secretion
INVENTOR(S): Bender, Paul E.; Loev, Bernard
PATENT ASSIGNEE(S): Smithkline Corp., USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

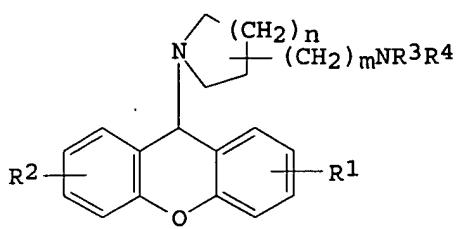
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| US 3980788 | A | 19760914 | US 1975-613689 | 19750915 |
| PRIORITY APPLN. INFO.: | | | US 1975-613689 | A 19750915 |
| IT 60717-46-6 | | | | |
| RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenolysis of) | | | | |
| RN 60717-46-6 CAPLUS | | | | |
| CN 3-Piperidinamine, N,N-dimethyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME) | | | | |



IT 60717-45-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)
RN 60717-45-5 CAPLUS
CN 3-Piperidinamine, N-methyl-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



GI



AB Pharmaceutical compns. having gastric acid secretion inhibitory activity comprising a pharmaceutical carrier and a xanthenylaminopiperidine or pyrrolidine compound (I: n = 1 or 2; m = 0, 1, 2, or 3; R1 = H, halogen, OH, lower alkyl, or lower alkoxy; R2 = H, halogen, lower alkyl, or lower alkoxy; R3 = lower alkyl; R4 = H, lower alkyl, or lower alkanoyl, or an acid addition salt) are reported. *Syntheses* of the compds: are also reported. E.g., 1-benzyl-3-piperidone [40114-49-6] was reacted with methylamine under **reducing** conditions and the resultant 1-benzyl-3-methylaminopiperidine [60717-45-5] reacted with formaldehyde under **reducing** conditions to give 1-benzyl-3-dimethylaminopiperidine [60717-46-6] which was hydrogenolyzed to give 3-dimethylaminopiperidine [50534-49-1]. Me isocyanate [624-83-9] was reacted with xanthydrol [90-46-0] and the resultant 9-(N-methylcarbamoyloxy)xanthene [30190-26-2] hydrolyzed and acetylated to give 9-acetoxyxanthene [35598-76-6]. The 9-acetoxyxanthene and 3-dimethylaminopiperidine were reacted to give 1-(9-xanthenyl)-3-dimethylaminopiperidine (II) [60717-47-7] which was incorporated into capsules containing II 200, lactose 75, and Mg stearate 5 mg.

L7 ANSWER 52 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1976:446289 CAPLUS

DOCUMENT NUMBER: 85:46289

TITLE: Rearrangements during the **synthesis** of substituted 1-benzylpyrrolidines and 3-substituted 1-benzylpiperidines

AUTHOR(S): Moragues, Jacinto; Prieto, Jose; Spickett, Robert G. W.; Vega, Armando

CORPORATE SOURCE: Inst. Invest., Lab. Almirall S. A., Barcelona, Spain
SOURCE: Journal of the Chemical Society, Perkin Transactions

1: Organic and Bio-Organic Chemistry (1972-1999)
(1976), (9), 938-40

CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal

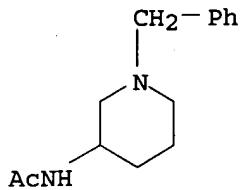
LANGUAGE: English

OTHER SOURCE(S): CASREACT 85:46289

IT 60169-74-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacetylation of)

RN 60169-74-6 CAPLUS

CN Acetamide, N-[1-(phenylmethyl)-3-piperidinyl]- (9CI) (CA INDEX NAME)

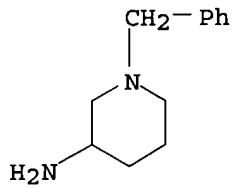


IT 60407-35-4P

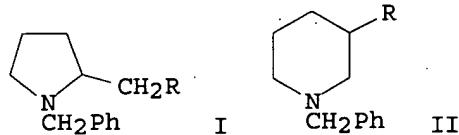
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 60407-35-4 CAPLUS

CN 3-Piperidinamine, 1-(phenylmethyl)- (9CI) (CA INDEX NAME)



GI



AB Treatment of 1-benzyl-2-(chloromethyl)pyrrolidine I (R = Cl) or 1-benzyl-3-chloropiperidine II (R = Cl) with NaN₃ gave a mixture of azides I and II (R = N₃) which on reduction gave a 50:50 mixture of I and II (R = NH₂). The interconversion of I and II (R = N₃) occurred via an aziridine intermediate. I (R = NH₂) was prepared independently from N-benzylproline and II (R = NH₂) from 3-acetamidopiperidine.

L7 ANSWER 53 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1976:38589 CAPLUS

DOCUMENT NUMBER: 84:38589

TITLE: Conformationally restricted analogs of histamine H1 receptor antagonists, trans- and cis-1-benzyl-3-dimethylamino-6-phenylpiperidine

AUTHOR(S): Ahmed, Ahmed E.; Hanna, Patrick E.; Grund, Vernon R.

CORPORATE SOURCE: Dep. Pharmacol., Univ. Minnesota, Minneapolis, MN, USA

SOURCE: Journal of Medicinal Chemistry (1976), 19(1), 117-22

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 84:38589

IT 57588-85-9P 57588-98-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

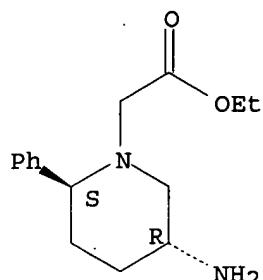
10/717, 958

(preparation and cyclization of)

RN 57588-85-9 CAPLUS

CN 1-Piperidineacetic acid, 5-amino-2-phenyl-, ethyl ester, trans- (9CI) (CA INDEX NAME)

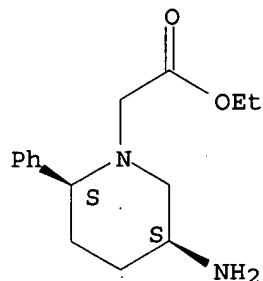
Relative stereochemistry.



RN 57588-98-4 CAPLUS

CN 1-Piperidineacetic acid, 5-amino-2-phenyl-, ethyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



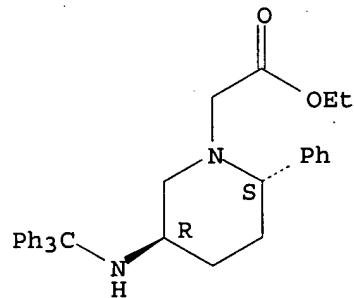
IT 57588-84-8P 57588-97-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and detritylation of)

RN 57588-84-8 CAPLUS

CN 1-Piperidineacetic acid, 2-phenyl-5-[(triphenylmethyl)amino]-, ethyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

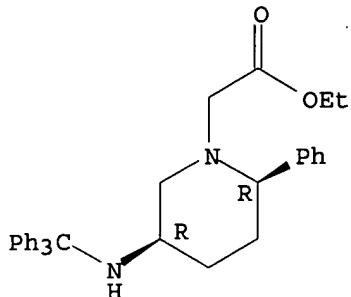


10/717, 958

RN 57588-97-3 CAPLUS

CN 1-Piperidineacetic acid, 2-phenyl-5-[(triphenylmethyl)amino]-, ethyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



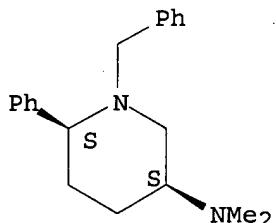
IT 57588-77-9P 57589-04-5P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation and pharmacol. of)

RN 57588-77-9 CAPLUS

CN 3-Piperidinamine, N,N-dimethyl-6-phenyl-1-(phenylmethyl)-, dihydrochloride, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

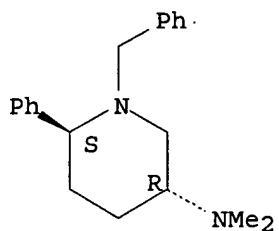


●2 HCl

RN 57589-04-5 CAPLUS

CN 3-Piperidinamine, N,N-dimethyl-6-phenyl-1-(phenylmethyl)-, dihydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● 2 HCl

IT 57588-86-0P 57588-89-3P 57588-90-6P
 57588-99-5P 57589-00-1P 57589-01-2P
 57589-02-3P 57589-03-4P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of)

RN 57588-86-0 CAPPLUS

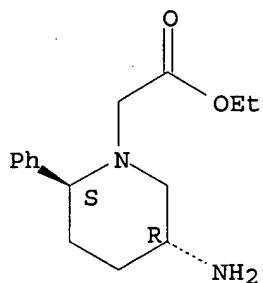
CN 1-Piperidineacetic acid, 5-amino-2-phenyl-, ethyl ester, trans-, diacetate
 (9CI) (CA INDEX NAME)

CM 1

CRN 57588-85-9

CMF C15 H22 N2 O2

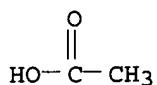
Relative stereochemistry.



CM 2

CRN 64-19-7

CMF C2 H4 O2

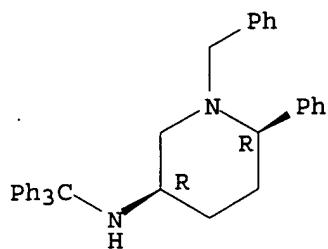


RN 57588-89-3 CAPPLUS

CN 3-Piperidinamine, 6-phenyl-1-(phenylmethyl)-N-(triphenylmethyl)-, cis-
 (9CI) (CA INDEX NAME)

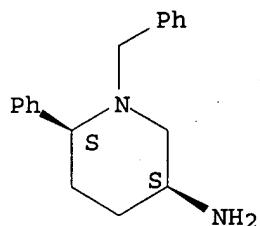
Relative stereochemistry.

10/717, 958



RN 57588-90-6 CAPLUS
CN 3-Piperidinamine, 6-phenyl-1-(phenylmethyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.

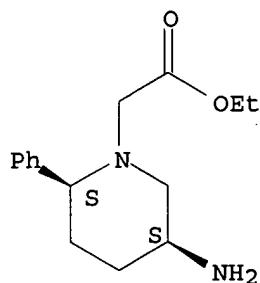


RN 57588-99-5 CAPLUS
CN 1-Piperidineacetic acid, 5-amino-2-phenyl-, ethyl ester, cis-, diacetate
(9CI) (CA INDEX NAME)

CM 1

CRN 57588-98-4
CMF C15 H22 N2 O2

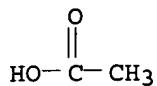
Relative stereochemistry.



CM 2

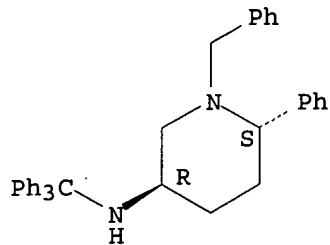
CRN 64-19-7
CMF C2 H4 O2

10/717, 958



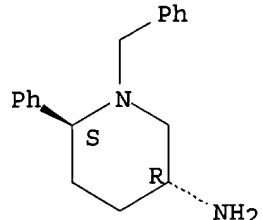
RN 57589-00-1 CAPLUS
CN 3-Piperidinamine, 6-phenyl-1-(phenylmethyl)-N-(triphenylmethyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



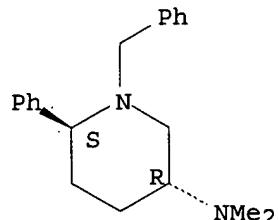
RN 57589-01-2 CAPLUS
CN 3-Piperidinamine, 6-phenyl-1-(phenylmethyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



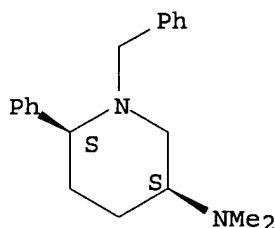
RN 57589-02-3 CAPLUS
CN 3-Piperidinamine, N,N-dimethyl-6-phenyl-1-(phenylmethyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



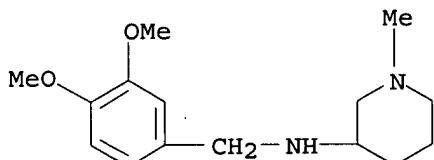
RN 57589-03-4 CAPLUS
CN 3-Piperidinamine, N,N-dimethyl-6-phenyl-1-(phenylmethyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



GI For diagram(s), see printed CA Issue.
 AB The *syntheses* of trans- [57589-04-5] and cis-1-benzyl-3-dimethylaminio-6-phenylpiperidine-2HCl (I) [57588-77-9] are described. Both isomers were found to be inhibitors of histamine, acetylcholine, and BaCl₂ induced contractions of the isolated guinea pig ileum. Neither isomer exhibited appreciable stereoselectivity in its ability to inhibit smooth muscle contractions. The cis compound was a more effective inhibitor of histamine-N-methyltransferase [9029-80-5] than the trans isomer.

L7 ANSWER 61 OF 68 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1961:144163 CAPLUS
 DOCUMENT NUMBER: 55:144163
 ORIGINAL REFERENCE NO.: 55:27301h-i,27302a-i,27303a-f
 TITLE: Application of sodium borohydride reduction to *synthesis* of substituted aminopiperidines, aminopiperazines, aminopyridines, and hydrazines
 AUTHOR(S): Walker, Gordon N.; Moore, Miriam Ann; Weaver, Barbara N.
 CORPORATE SOURCE: Ciba Pharm. Prods. Inc., Summit, NJ
 SOURCE: Journal of Organic Chemistry (1961), 26, 2740-7
 CODEN: JOCEAH; ISSN: 0022-3263
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 OTHER SOURCE(S): CASREACT 55:144163
 IT 132467-51-7, Piperidine, 1-methyl-3-veratrylamino-, dihydrochlorides (preparation of)
 RN 132467-51-7 CAPLUS
 CN Piperidine, 1-methyl-3-veratrylamino-, dihydrochloride (6CI) (CA INDEX NAME)



● 2 HCl

AB Quaternization of 4-aminopyridine (I) with alkyl and arylalkyl halides

gave 4-aminopyridinium salts, which were reduced with NaBH₄ to 1-(alkyl or arylalkyl)-4-aminopiperidines. Both 1-alkyl-4-aminopiperidines and 1-alkyl-4-aminopiperazines could be converted to Schiff bases, which were reduced with NaBH₄ to the corresponding secondary amines. Similar reduction of appropriate Schiff bases as a means of preparing substituted 3-aminopiperidines, aminopyridines, and aminomethylpyridines, as well as reduction of dialkylhydrazones to the corresponding trisubstituted hydrazines were also described. Anhydrous HBr was passed through a cold solution of 33.6 g. veratryl alc. in 500 ml. C₆H₆ 10 min., the lower layer separated, the C₆H₆ treated with Na₂CO₃, stirred, the solution of veratryl bromide (II) filtered, and used in the following step without purification. To the C₆H₆ solution of II was added 19 g. I; the mixture refluxed 1.5 hrs., filtered, and the product crystallized gave 54 g. 1-(3,4-dimethoxybenzyl)-4-aminopyridinium bromide (IIa), m. 248-50° (decomposition), (alc.). A simple two-step synthesis was used in the preparation of the 1,2-diphenylethyl- and 3,4-dimethoxyphenacyl-substituted compds. The remaining substances were prepared from the com. available bromo (in one case, iodo) compds. by the same procedure with a few modifications in solvents used and reaction times. In reactions involving α,ω -dibromoalkanes, a mixture of the compound, 2 equivs. I, and a suitable amount of PhMe was refluxed. The product often settled as an oil. In this case the supernatant was decanted, and the oil crystallized 2-Methyl-4-aminopyridine (III) was most conveniently synthesized by a 2-step reduction of 4-nitro-2-picoline N-oxide as follows. (A) The oxide (45 g.) in 200 ml. alc. containing 4 g. 10% Pd-C shaken under H at 45 lb./sq. in. gave 33 g. 2-methyl-4-aminopyridine N-oxide (IV), yellow crystals, m. 181-3° (alc.). IV (30 g.) in 300 ml. 1:1 AcOH-H₂O treated with excess Zn dust, the mixture warmed 1 hr., cooled, covered with Et₂O, treated with a 40% solution of 500 g. NaOH, and the Et₂O solution evaporated

gave 16.8 g. III, m. 95° (cyclohexane). The following (4-H₂NC₅H₄N)RBr were obtained (R, solvent prepared in, reflux time in hrs., % yield, and m.p. given): EtO₂CCH₂, C₆H₆-alc., 1.5, 92, 197°; EtO₂CCH₂CH₂, PhMe, 5, 73, 159°; HOCH₂CH₂, PhMe, 3.5, 80, 131°; PhCH₂, C₆H₆, 0.5, 90, 196°; Ph₂CH, PhMe, 3, 56, 263°; PhCH₂CH₂, PhMe, 2, 77, 260°; PhCH₂CHPh, C₆H₆, 9, 53, 245°; PhOCH₂CH₂, PhMe, 4.5, 75, 184°; BzCH₂, C₆H₆, 2, 96, 308°; 3,4-(MeO)C₆H₃COCH₂, C₆H₆-alc., 0.3, 64, 271°; p-O₂NC₆H₄CH₂, PhMe, 5.5, 66, 266°; 2,4-(O₂N)C₆H₃, PhMe, 1, 56, 294°. The following [4-H₂NC₅H₄N(CH₂)_nNC₅H₄-4]Br₂ were similarly obtained (n, solvent, reflux time, % yield, and m.p. of product given): 4, PhMe, 2, 87, 273°; 6, PhMe, 14, 91, 303°; 8, PhMe, 5.5, 84, 300°; 9, PhMe, 5, 14, 221°; 10, PhMe, 5, 88, 247°; 11, PhMe, 7.5, 48, 216°; 12, PhMe, 13, 29, 209°; 16, PhMe (prepared from alkyl iodide), 11, 94, 185°. The following [2,4-Me(H₂N)C₅H₄N(CH₂)_nNC₅H₄(NH₂)Me-4,2]Br₂ were obtained (n, solvent, reflux time in hrs., % yield, and m.p. given): 8, PhMe, 8, 60, 304°; 9, PhMe, 9, 17, 275°. IIa (30 g.) in 700 ml. MeOH treated in 1 hr. with 250 g. NaBH₄, the mixture heated on a steam bath, cooled, treated with 500 ml. H₂O, covered with 2 l. Et₂O, the 2 phases treated with anhydrous K₂CO₃ to convert the lower layer to a paste, the Et₂O separated, evaporated, the 20 g. oil dissolved in 30 ml. alc., and treated with dry HCl gave 12.2 g. 1-(3,4-dimethoxybenzyl)-4-aminopiperidine-2HCl, m. 223-5° (decomposition) (MeOH-Et₂O). Other 4-aminopiperidines were obtained from the resp. quaternary salts by the same procedure. The free bases were hygroscopic oils. The amines had to be salted out with NaCl. When 4-aminopiperidines, as free bases, were required for further work, they were used directly in the crude state. 1-Methyl-4-aminopiperidine and 1-(β -hydroxyethyl)-4-aminopiperidine, both formed hygroscopic salts with HCl. The following

4-(N-substituted-amino)piperidine-2HCl were thus obtained (R, % yield, and m.p. given): EtO₂CCH₂, 17, 169°; PhCH₂, 41, 255°; PhCH₂CH₂, 88, 321°; PhCH₂CHPh, 40, 237° (decomposition); PhOCH₂CH₂, 44, 220°; PhCH(OH)CH₂, 90, 248° (decomposition); 3,4-(MeO)C₆H₃CH(OH)CH₂, 56, 220° (decomposition); p-O₂NC₆H₄CH₂, 10, 265° (decomposition). The following 4-H₂NC₅H₄N(CH₂)_nNC₅H₄NH₂-4·4HCl were similarly obtained (n, % yield, and m.p. given): 6, 22, 204°; 10, 16, 295°; 12, 34, 311°; 16, 20, 315°.

1,10-Bis(4-amino-1-piperidyl)decane was also characterized by preparation of the bis(dichloroacetate)-2HCl, m. 227-30° (decomposition) (alc.).

1-Methyl-4-aminopiperazine (8.1 g.) and 11.2 g. veratraldehyde in 200 ml. PhMe refluxed 1.5 hrs., evaporated, the residue dissolved in 150 ml. MeOH, the solution reduced with 40 g. NaBH₄, heated 0.5 hr. on the steam bath, and the 20.5 g. yellow oil treated with alc. HCl gave 10 g. 1-methyl-4-(3,4-dimethoxybenzylamino)piperazine, m. 199-202° (decomposition). Other secondary aminopiperidines and aminopiperazines were given in a table. Attempts to reduce imines derived from 1-phenyl-2-propanone and 1-substituted 4-aminopiperidines with NaBH₄ did not lead to desired products, probably because of cleavage of the unstable imines.

3-Aminopyridine (16.8 g.) and 30 g. veratraldehyde in 500 ml. xylene refluxed 24 hrs. and the 45.5 g. residual oily imine in MeOH reduced with NaBH₄ gave 33 g. 3-(3,4-dimethoxybenzylamino)pyridino (V), m. 123-5° (MeOH). The other pyridines were similarly prepared.

The following RNHR' were thus obtained (R, R'; % yield, and m.p. given): 3,4-dimethoxybenzyl, 1-methyl-4-piperidyl, 60, 254-6° (decomposition); 3,4,5-trimethoxybenzyl, 1-methyl-4-piperidyl, 37, 264-5° (decomposition); 3,4-dimethoxybenzyl, 1-(β-hydroxyethyl)-4-piperidyl, 12, 255-6° (decomposition); 4-methoxybenzyl, 1-(3,4-dimethoxybenzyl)-4-piperidyl, 46, 274-5° (decomposition); 3,4,5-trimethoxybenzyl, 1-methyl-4-piperazyl, 56, 135-7°; p-dimethylaminobenzyl,

1-methyl-4-piperazyl, 40, 125-7° (157-60°); 3-pyridylmethyl,

1-methyl-4-piperazyl, 95, 201-2° (220-6° with 0.5H₂O);

1-hydroxy-1-phenyl-2-propyl, 1-methyl-4-piperazyl, 25, 219-21° (decomposition); 3,4-dimethoxybenzyl, 2-pyridyl, 65, 102-3°;

3,4,5-trimethoxybenzyl, 2-pyridyl, 45, 167-8°; p-

dimethylaminobenzyl, 2-pyridyl, 52, 125-6°; 3,4,5-trimethoxybenzyl,

3-pyridyl, 63, 109-10°; 3,4,5-trimethoxybenzyl, 3-pyridylmethyl,

90, 205-7°; p-dimethylaminobenzyl, 3-pyridylmethyl, 96,

185-6° (decomposition); 3,4-dimethoxybenzyl, 4-pyridylmethyl, 22,

200° (decomposition); 3,4,5-trimethoxybenzyl, 4-pyridylmethyl, 43,

214-16°; p-dimethylaminobenzyl, 4-pyridylmethyl, 45, 195-6°;

1-phenyl-2-propyl, 3-pyridylmethyl, 55, 205-7°; 1-phenyl-2-propyl,

4-pyridylmethyl, 80, 181-3°; 3,4,5-trimethoxybenzyl, NMe₂, 45,

81-3; p-dimethylaminobenzyl, NMe₂, 7, 158-61° (decomposition);

1-phenyl-2-propyl, NMe₂, 70, 123-5°; 1,2-diphenylethyl, NMe₂, 23,

183-5°; PhCH:CHCHMe, NMe₂, 5, 117-20° (decomposition). V (14.1

g.) converted rapidly to the MeI salt, evaporated, the crystals suspended in 200 ml. MeOH, reduced with 125 g. NaBH₄, and the residual oil treated with

HCl gave 14.6 g. 1-methyl-3-(3,4-dimethoxybenzylamino)piperidine-2HCl, m.

233-5° (decomposition). 3-Aminopiperidine (7.6 g.), 12.7 g.

veratraldehyde, and 250 ml. PhMe refluxed 3.5 hrs., the crude imine

reduced with NaBH₄ in alc., and crystallized gave 20.6 g. V·2HCl, m.

229-31° (alc.). Reduction of p-dimethylaminobenzylidene

derivative and isolation gave 76% 3-(4-dimethylaminobenzylamino)piperidine, no definite m.p. 3-(3-Pyridylmethylamino)piperidine was obtained in 79% yield

by reduction of the 3-pyridylidene derivative and isolated as the

tri-HCl salt. Veratraldehyde (16.3 g.) and 6.5 g. N,N-dimethylhydrazine

mixed, the oil taken up in 200 ml. C₆H₆, the solution refluxed 4 hrs.,

evaporated, and the hydrazone reduced in MeOH with NaBH₄ gave 13.9 g.

N,N-dimethyl-N-(3,4-dimethoxybenzyl)hydrazine-HCl, m. 172-4.5°.

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The other hydrazine derivs. above were prepared by the same method

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COST IN U.S. DOLLARS | SINCE FILE
ENTRY | TOTAL
SESSION |
|--|---------------------|------------------|
| FULL ESTIMATED COST | 387.54 | 549.08 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE
ENTRY | TOTAL
SESSION |
| CA SUBSCRIBER PRICE | -52.56 | -52.56 |

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